

**INTERNATIONAL CONFERENCE ON HARMONISATION OF  
TECHNICAL REQUIREMENTS FOR REGISTRATION OF  
PHARMACEUTICALS FOR HUMAN USE**

**ICH M2 EWG**

**Electronic Common Technical Document Specification**

This specification has been developed by the ICH M2 Expert Working Group in accordance with the ICH Process as pertains to the M2 EWG.

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## **ICH eCTD Specification**

### ***Introduction***

The ICH M4 Expert Working Group has defined the Common Technical Document (CTD). The ICH M2 Expert Working Group has defined, in the current document, the specification for the Electronic Common Technical Document (eCTD). The eCTD is defined as an interface for industry to Agency transfer of regulatory information while at the same time taking into consideration the facilitation of the creation, review, lifecycle management and archival of the electronic submission. The eCTD specification lists the criteria that will make an electronic submission technically valid. The focus of the specification is to provide the ability to transfer the Marketing Application electronically from industry to a regulatory authority. Industry to industry and Agency to Agency transfer is not addressed.

The specification is divided into main chapters followed by a number of appendices in which detailed technical specifications are given. It will provide a mechanism whereby parts of the specification will be updated or adjusted to agreed new technologies or standards on an independent basis without the necessity of updating it all. This aspect will be covered in the chapter Change Control.

### ***Background***

The specification for the eCTD is based upon content defined within the CTD issued by the ICH M4 EWG. The CTD describes the organisation of modules, sections and documents. The structure and level of detail specified in the CTD has been used as the basis for defining the eCTD structure and content but where necessary, additional details have been developed within the eCTD specification.

The philosophy of the eCTD is to utilise open standards. Open standards, including proprietary standards, which through their widespread usage can be considered defacto standards, are deemed to be acceptable in general.

### ***Scope***

The CTD as defined by the M4 EWG does not cover the full submission that is to be made in a region. It describes only modules 2 to 5, which are common across all regions. It does not describe the content of module 1 the Regional Administrative Information and Prescribing Information nor does it describe documents that may be submitted as amendments or variations to the initial application.

The value of production of a specification for the creation of an electronic submission based only upon the modules described in the CTD would be limited. It has been necessary to produce a specification for the eCTD that is applicable to all modules of initial marketing applications and for other submissions of information throughout the lifecycle of the product, such as variations and amendments.

This document describes the parts of the Marketing Application that are common to all regions and some of the lifecycle requirements for products. The parts of the Marketing

Applications that are specific to a region will be covered by regional guidances. However, the backbone has been developed to handle both the regional and common parts of submissions.

### ***Requirements***

The specification is designed to support high-level functional requirements such as the following :

- Copy and paste
- Viewing and printing of documents
- Annotation of documentation
- Facilitate the exporting of information to databases
- Searching within and across applications
- Navigation throughout the eCTD and its subsequent amendments/variations

### ***Change Control***

#### **INTRODUCTION**

The specification for the eCTD is likely to change with time. Factors that will affect the content of the specification include, but are not limited to:

- Change in the content of the CTD, either through the amendment of information, at the same level of detail, or by provision of more detailed definition of content and structure
- Change to the regional requirements for applications that are outside the scope of the CTD
- Updating of standards that are already in use within the eCTD
- Identification of new standards that provide additional value for the creation and/or usage of the eCTD
- Identification of new functional requirements
- Experience of use of the eCTD by all parties

The first specification for an eCTD is an ICH M2 Step 4 document. The eCTD Specification describes how to prepare, submit and archive an electronic submission using readily available and cost effective tools and formats. The Specification also includes an appendix for each module of the CTD. Each appendix consists of (or includes) detailed information for the structure and format to be used in preparing a CTD module.

It is understood that technology will continue to evolve at a rapid pace. There may also be changes to the CTD. Information technology capabilities and requirements will also evolve in the pharmaceutical industry and in the regulatory authorities. The change control process described in this section allows the eCTD Specification to be updated to meet new requirements and to take advantage of technology improvements. Each appendix should be updated as needed, independent of the remainder of the document.

## **PROCESS**

The eCTD Specification Change Control Board (CCB) is authorized by the ICH Steering Committee to make changes to the eCTD Specification to keep pace with advancing technology. Since the issuance of guidelines is the responsibility of the regulatory authorities, in line with the standards ICH process, the regulatory authorities are the voting members of the CCB. Industry representatives from each of the three regions, and Health Canada as observer, are non-voting members of the change control board. The position of chair of the CCB rotates on an annual basis among the regulatory authority members.

The three regulatory authorities represented in the ICH M2 Expert Working Group are responsible for initiating changes to the eCTD Specification, based on industry or regulatory input. A change may be proposed by any of the regulatory authorities. A group or individual, not a member of an ICH regulatory authority, can propose a change to the specification, including recommendation for experts to be invited, by submitting the proposal to one of the regional regulatory authorities.

The CCB meets on a regular schedule to discuss, evaluate and agree on proposed changes to the specification. During these meetings the members of the CCB and other invited parties evaluate the proposed changes. The decision to accept a change to the eCTD Specification is made by a unanimous vote of the regulatory authority representatives.

The agreed changes to the specification are published for public comment in each region. Comments are collected and considered by the CCB and are adopted in modified or unmodified form or rejected. The updated eCTD Specification is agreed upon and signed by the three regional regulatory authorities, and is published as required in each region. The planned implementation date and transition period for each change in each region is included in the published description of the change. Adopted changes are published on an annual basis except for emergency changes, e.g. an error in critical metadata, as defined by the CCB which will be published immediately upon adoption. The CCB will provide guidance that will indicate how existing submissions and those currently undergoing late stage-compilation should be updated.

Regulatory authorities will support submissions described by at least two consecutive versions of the eCTD Specification. All versions of the specification will be kept by the regulatory authority as long as needed to process eCTD submissions that are on file with a regulatory authority.

The CCB will establish its meeting schedule at the first meeting of the CCB. The first meeting will be at the same time as the ICH Steering Committee.

## **PROCEDURE**

Change requests should be submitted to a regulatory authority. Change requests received at least 30 days before a scheduled CCB meeting will be placed on the agenda for that

meeting. Change requests received less than 30 days before a CCB meeting will be placed on the agenda for the following meeting.

Change requests should contain as much of the following information as possible:

- A description of the problem that the change is intended to solve.
- The proposed solution(s) – this consists of a description of the solution(s) and the text of the changes to affected documents.
- A detailed description of any testing or research that was done to support the solution(s) being proposed.

The CCB will maintain a public list of requests and the status of each request. New change requests will be posted to the list within 30 days of their receipt.

### ***Approach to Documentation and Use of the eCTD Specification***

The approach to the management of the specification for the eCTD is to divide the documentation into a series of independent but related appendices. This will facilitate the maintenance of the specification, as it will not require that all documentation be updated even for a small change to one part of the specification. Each appendix can be updated independently as and when required, thus being able to more readily support the currency of the specification as a whole.

## **Appendix 1 Overall Architecture**

### ***Guiding Design Principles***

This paragraph defines the basic principles that drove the design and architecture of the eCTD. Detailed specifications are defined in appendices 2 and 11.

### ***Business Model***

The business process to be supported can be described as follow:

Industry <-----> Message <-----> Agency

The business process defines specific requirements for the message.

The primary focus of the eCTD is to provide a data interchange message between the industry and agencies. The industry initiates the process by creating the initial message in terms of an electronic CTD. Throughout the lifecycle of this process, additional information will be submitted to update or modify the information contained in the initial message e.g. supplement, amendment, variation etc. The agency will submit acknowledgements, queries and requests to the industry. These are considered simple messages utilizing electronic mail or other transport formats as defined in appendix 8. The data interchange message should support this two-way stream and contain sufficient information to support lifecycle management at both the industry and agency ends.

The overall architecture of the eCTD is designed to provide a commonly agreed upon message and message structure that imposes minimal restriction to the industry and agencies.

### ***Modular Structure of the eCTD***

The structure of the electronic submission in terms of organization and navigation should be consistent with the modular structure of the Common Technical Document. The goal of this design principle is to standardize the electronic format of the common parts of the eCTD.

### ***XML Based Backbone***

The XML Backbone Instance defines the overall structure of the submission. The purpose of the XML instance is two-fold: (1) to manage **meta** data for the entire submission and each document within the submission and (2) to constitute a comprehensive table of contents and provide corresponding navigation aids. **Meta** data on submission level includes information about submitting and receiving organization, manufacturer, publisher, ID and kind of the submission, and related data items. Examples for **meta** data on document level are versioning information, language, descriptive information such as document names, timestamps, etc. Details are defined in appendix 11.

The XML instance of any submission should be designed and validated according to the Document Type Definition (DTD) as defined in appendix 14.

The DTD describes the hierarchical structure according to the CTD as defined by the ICH-M4 expert working group. It includes multiple hierarchical levels depending on the specific module as defined in the CTD. The actual submission may include more hierarchical levels below those defined in the CTD. The XML backbone instance covers the entire submission including all hierarchical levels and includes references to each individual file.

The submission should include a style sheet that supports presentation of the XML instance, navigation according to the table of contents and provides access to all documents within the submission. A standard style sheet is defined and provided by the ICH-M4 expert working group. Presentation and navigation via other style sheets on the receiving side should be possible.

The physical folder structure of the submission follows the hierarchical structure. Child-sections are implemented as folders within parental sections. For modules 2 through 5 this structure is mandatory at least for the first two levels of the table of contents which are called modules and sections. The directory structure below the section level may be specified by the applicant. For module 1 (administrative and labeling information) regional guidelines for the directory structure may apply.

The XML instance includes for each document a reference to the physical file within the folder structure. The XML instance includes attributes for descriptive names of folders and documents. Therefore, the names of directories and files are not required to be descriptive or include meta data. Navigation is primarily support via descriptive attributes in the XML backbone instance.

### ***Multiple Region Support***

The scope of each submission is global according to the Common Technical Document, meaning that modules 2 through 5 of a submission are intended for all regions with the exception of selected documents (e.g. in the quality module), which will have a regional scope. Module 1 of a submission will be regional in nature.

The DTD as defined by the ICH-M2 expert working group specifies the structure of the common parts of the eCTD primarily focussing in module 2 through 5. It allows to link to regional DTDs for module 1 which will be defined by the authorities in each region.

Accordingly, each submission will include files with a global scope and those intended for one of more regions only. The applicant may decide to omit region specific files from submissions that do not apply to the specific scope. For example, a submission should include SAS data sets as required in the United States. Those documents may not be included for submissions in Europe and Japan.

### ***Multiple Language Support***

The same document may exist in multiple language versions. Even more, a single document may include more than one language. The actual language of a document

should be specified as a meta data item in the XML instance. If a document includes more than one language then there are multiple language related meta data items in the XML instance. File names are not required to include information about the language of a document.

### ***Lifecycle Management***

The applicant creates a submission that is stored in a local repository. The applicant submits the initial submission to the agency, which imports the submission into another local repository. The nature and kind of the local repositories is not within the scope of the eCTD. The initial submission should be self-contained meaning that it includes all documents and no references to other submissions. Regional guidance should be consulted if references to other submissions are needed.

Following to the initial submission, the applicant may submit incremental updates such as amendments and variations. Updates may refer to documents in the previous submissions. Updates should be designed in a way that they can be loaded into the repository by fully preserving the initial or previous submission via version control. The XML instance should include meta data identifying the update and providing navigation aids to filter for different submission types.

When a Common Technical Document is submitted electronically, the entire submission should be in electronic form with the exception of certain regional forms that currently require written signatures. See Appendix 9 for regional requirements. There should be no eCTD submissions that consist of a combination of electronic and paper files.

## **Appendix 2 The eCTD Submission**

### ***Introduction***

This appendix specifies the Information Technology aspect of the eCTD Submission. Informally, the eCTD Submission is a directory structure with files in several formats including the XML backbone and files containing reports, data and other submission information. The eCTD Submission supports multilingual and multi-region aspects.

### ***The eCTD Submission***

An eCTD Submission is a collection of data objects that follows the eCTD Specification. The main function of the eCTD Submission is data transmission. Information systems would have to be created to process the eCTD Submission. The biggest benefits are expected when the eCTD Submission is loaded into an information system that supports the review process. However, one can view an eCTD Submission with a web browser as it is web ready. In the web environment, the eCTD Submission should be consumable as is at least in the following ways:

- Standalone: Viewable with a web browser.
- Network: Loadable into a web server.

### ***Structure***

The eCTD Submission is composed of the following:

- Directory Structure
- Backbone

## **DIRECTORY STRUCTURE**

The Directory Structure is a structure of directories and files that could be in several formats. There should be a reasonable maximum number of entries (directories and files) per directory. The Directory Structure should follow the rules below. The files could be in several formats as specified below.

The name of the files and directories are identifiers. They should be short. The file names are not intended to convey metadata, though some meaning in the names helps; i.e., no random names. Directory or file names should be the same as the element names, or a very near approximation according to the rules below.

Directory names required by the Backbone are fixed. Some of the directories and files are optional. Every directory could contain a directory named **sponsor** for additional directories and/or files not foreseen in this specification. The directories and files and the directories **sponsor** should follow the naming rules. Directory names that are added to the eCTD Submission by the sponsor should be descriptive and logical.

## **BACKBONE**

The Backbone is a valid XML document. It is in the Root Directory. The Root Directory should contain at least two files and one or more directories. One of the files in the Root Directory is the Backbone and the other is the MD5 checksum of the Backbone. The Backbone is the starting file for the processing by an XML processor.

The intention is to have links from the Backbone to Leaf files in the eCTD Submission as opposed to creating a single XML document that contains the entire eCTD Submission. The Backbone should contain mostly linking facilities to the Leaves. The Backbone can contain other data, such as metadata.

### ***eCTD Template***

The eCTD Template is an empty directory structure with the recommended style sheets. It is an illustration an eCTD Submission and it is ready to be populated with the sponsor data.

### ***Representation***

In an eCTD Submission, the same information could be represented in different fashions. The aspects considered are:

- Format: e.g., PDF, XML
- Language: e.g., English, Japanese

Note the difference between:

- Document: it refers to the content, independently of the representation; e.g., mydoc.
- File: it refers to physical storage; e.g., mydoc.pdf.

Several representations of the same document could be present. For example, the document mydoc could be present as mydoc.xml and mydoc.pdf.

Source Format is the format of the original document before transformation. For example, mydoc.doc is the Source Format of a document produced in Word and mydoc.rtf is a transformation of the document Saved as RTF. Information could be lost in transformations.

### ***Formats***

Formats should be readable at least for as long as it is needed for the regulatory process. This process could be very long; e.g. 50 years. This points to neutral formats: formal standard, industrial standard, vendor independent, text-like, etc. The format should be adapted to the type of data.

There could be rules on how to use the different formats. These rules are in the appropriate appendices of this specification.

The list of accepted formats will be updated as technology evolves and new requirements arise. XML will be the preferred format for all types of data. At present, it is

recommended to use XML as much as it is reasonably possible; at least the following should be considered: Extensible Stylesheet Language (XSL), Scalable Vector Graphics (SVG) and Chemical Markup Language (CML).

## COMMON FORMATS

The Common Formats that can be included in an eCTD Submission are:

- Narrative: Portable Document Format (PDF)
- Structured: Extensible Markup Language (XML)
- Graphic: Whenever possible, use PDF. When required, use Joint Photographic Experts Group (JPEG), Portable Network Graphics (PNG) and Graphics Interchange Format (GIF). Special formats for very high resolutions may be needed on a case-by-case basis.

## REGIONAL FORMATS

Regulatory authorities and applicants could agree in the use Regional Formats; i.e., non Common Formats or uses of the Common Formats in a different way from above. The use of Regional Formats is discouraged and the intention is to use as much as possible the Common Formats. The intention of the Regional Formats is mostly for transition.

There are two classes of transitions:

- Legacy Transition: from the past to the present; i.e., old formats to present formats.
- Future Transition: from the present to the future; i.e., from present formats to new formats. The new formats would normally be candidates for Common Formats.

Rich Text Format (RTF) and XML (with presentation) have been considered for Regional Formats. Regional guidance will specify the Regional Formats, including where in the dossier they can be used.

### ***Languages***

The (natural) language of the file could be indicated in the following way:

DocumentName-LanguageCode.Extension

LanguageCode are two characters code from ISO-639 (ISO-639).

For example:

hello-en.pdf	English in PDF
hello-jp.pdf	Japanese in PDF
hello-jp.xml	Japanese in XML
hello-jp.xml	Japanese in XML
hello.pdf	PDF (language not indicated)

The intention of the language indicators is only to facilitate the creation of file names. It is not metadata. The metadata is contained as indicated in the relevant sections of the eCTD specification. If there is a conflict, the metadata should be followed and the language indicator in the file.

### ***Links***

Links among objects in the eCTD Submission should be relative. The intention is to make the eCTD Submission self-contained. There could be absolute links to other external objects. These would probably be references.

One can always point to a file. The capacity to point to a specific location within a file depends on the linking technology. Different formats allow for the use of different linking technology. The rules on linking technologies are in the appendices of the formats.

The content part of the linking is in the appendix Preparation of the eCTD (appendix 11); i.e., from where to where the linking should go.

### ***Presentation***

Similar to linking technology, presentation is closely associated with formats. To associate a style sheet with a file usually one has to use a linking technology. The linking between style sheet (that could be in a separated file) and a data file should be relative. In addition, there is the dimension of media. One file could have several style sheets; the one used depends on the media. For example, there could be one presentation for the screen and another for paper.

Standard eCTD Style Sheets should be developed at least for the most popular formats and media. For example, XML used for the screen and for paper. For paper format, XSL (with formatting objects) for transformation into PDF should be considered.

### ***Checksums***

The eCTD Submission should contain checksums for each individual file and one for the whole eCTD Submission. Initially, the MD5 Message-Digest Algorithm (MD5) should be used for this purpose. Other techniques could be used in the future. Including a checksum for each individual file provides a number of benefits including:

- The integrity of each file can be verified by comparing the checksum submitted with the file and the computed checksum.
- The checksum can be used to verify that the file has not been altered in the historical archive of the regulatory authority. This is especially useful as the files are migrated from one storage medium to another, as in the case of backup to magnetic tape storage.
- The checksum can be used as a unique identifier for each file in the submission in cases where there is a question between the sponsor and the regulatory authority as to which physical file is in an eCTD submission.

### ***Element to file directory mapping***

Follow these rules:

- The rules below for the file and directories take precedence.
- Ideally, the element and file/directory name should be the same.
- Add the corresponding extension to the file.
- If needed, use a reasonable abbreviation.

### ***File extension***

All files should have one and only one file extension; i.e., zero extension is not allowed and two or more is not allowed. The file extension should be used to indicate the format of the file. For example:

hello.pdf	PDF
hello.rtf	RTF

Encoded files should have the appropriate extension of the encoding mechanism. As only one extension is allowed, the original extension should be transformed. For example, hello.pdf should become hello-pdf.zip.

The mapping between formats and extensions are:

#### IANA nomenclature

text/css	css
text/html	html or htm
text/xml	xml
application/pdf	pdf
application/rtf	rtf
application/vnd.ms-excel	xls
image/jpeg	jpg
image/png	png
image/gif	gif

#### Non IANA nomenclature

DTD	dtd
XPT (SAS)	xpt
XSL	xsl

The eCTD Submission could use formats not registered with the Internet Assigned Numbers Authority (IANA).

The presence of a format in this list does not imply that it is an acceptable format. For formats absent from this list, widely used mapping between the formats and the extensions should be used.

Future direction: if a mechanism (e.g., standard) becomes available that associates the formats with file extension, it should be considered for this specification.

## ***Name***

*Name* is a token composed of the following characters:

- Letters "a" to "z", "A" to "Z" [U+0061 to U+007A, and U+0041 to U+005A].
- Digits "0" to "9" [U+0030 to U+0039].
- "-" [HYPHEN-MINUS, U+002D].
- "\_" [LOW LINE, U+005F].

The notation "U+" refers to the Unicode [UNICODE] notation.

Correct Names (only the Name without the extension):

part\_a  
part-b  
myfile  
hello

Incorrect Names (only the Name without the extension):

part a (' ; SPACE is not allowed)  
myfile.xml (' ; FULL STOP is not allowed)  
hello:pdf (' ; COLON is not allowed)

Directory Name is a Name.

File Name is one Name followed by one Name separated by a '.' (FULL STOP, U+002E).

Correct File Names (with the extension):

a\_part.xml  
myfile.pdf  
hello.cml

Incorrect File Names (with the extension)::

a part.pdf (' ; SPACE is not allowed)  
hello (missing extension)  
hello:xml (' ; COLON is not allowed)

The maximum length of a Directory Name or a File Name is 256 characters.

Document Name is the first Name in the File Name. For example, docname in the File Name docname.ext.

## ***Character encoding***

The character encoding (charset) in order of preference are:

- Unicode UTF-8, Unicode 16 bits [ISO-10646].
- ISO-8859-1 (Latin-1) or appropriate ISO-8859-x; e.g., ISO-8859-7 for Greek.
- The appropriate SHIFT\_JIS.

- Other character encodings. They should be appropriate to the language and widely available.

## ***References***

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<http://www.xml-cml.org>

[CSS2] *Cascading Style Sheets, level 2*

<http://www.w3.org/TR/REC-CSS2>

[ECMAScript] *ECMAScript Language Specification*, 3<sup>rd</sup> edition. ECMA- 262

<http://www.ecma.ch/ecma1/STAND/ECMA-262.HTM>

[EXCEL] Microsoft Excel

<http://www.microsoft.com/office/excel/default.htm>

[GIF] *Graphics Interchange Format*

<http://tronche.com/computer-graphics/gif/gif89a.html>

[HTML] *HTML 4.01 Specification*

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[IANA] Internet Assigned Numbers Authority

<http://www.iana.org>

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<http://www.jpeg.org/public/wg1n1807.txt>

[MD5] *The MD5 Message-Digest Algorithm*

<http://ietf.org/rfc/rfc1321.txt>

[PDF] *Portable Document Format*

<http://partners.adobe.com/asn/developer/technotes.html#pdfspec>

[PNG] *PNG (Portable Network Graphics) Specification Version 1.0*  
<http://www.w3.org/TR/REC-png.html>

[RTF] *Rich Text Format (RTF) Specification, version 1.6*  
<http://msdn.microsoft.com/library/specs/rftspec.htm>

[SVG] *Scalable Vector Graphics (SVG) 1.0 Specification* (work in progress)  
<http://www.w3.org/TR/1999/WD-SVG-19991203>

[UNICODE] Unicode Consortium  
<http://www.unicode.org>

[XHTML] *XHTML 1.0: The Extensible HyperText Markup Language*  
<http://www.w3.org/TR/WD-html-in-xml>

[XML] *Extensible Markup Language (XML) 1.0 (Second Edition)*  
<http://www.w3.org/TR/REC-xml.html>

[XSL] *Extensible Stylesheet Language (XSL)*  
W3C Candidate Recommendation 21 November 2000 (work in progress)  
<http://www.w3.org/TR/WD-xsl>

[XSLT] *XSL Transformations*  
<http://www.w3.org/TR/xslt.html>

## **Appendix 3 File Organisation for the eCTD**

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
		<i>(Uses CTD numbering scheme, always begins with a letter 'm' so as to meet XML standards for element names, uses lower case for consistency and uses hyphen throughout to avoid repeating 'periods') n/a = not applicable</i>	<i>(Generally matches CTD section title, but is restricted to 32 characters including 'period' and 3 character file extension if required - all lower case with underscore between words).</i>	<i>(Identifies universally acceptable file types plus additional, allowable file times)</i>	<i>(Comment to help guide the applicant in understanding the construction of the eCTD)</i>
			<i>n/a = not applicable Items in italics are examples and applicants may use the terminology they require so long as it adheres to the file naming conventions</i>		
Module 1	Regional Administrative Information	module-1	module_1	Folder name only	Folder name only means that it is just a folder in the hierarchy and not a file with content
A	Module 1 Table of Contents	n/a	n/a	Not required in eCTD	The 'Table of Contents' is created from the XML backbone description and the stylesheet applied
B	Documents specific to each region (for example, application forms, prescribing information)	m1-b	as defined in regional requirements	Regional specification as defined in regional requirements	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
		<i>(Uses CTD numbering scheme, always begins with a letter 'm' so as to meet XML standards for element names, uses lower case for consistency and uses hyphen throughout to avoid repeating 'periods') n/a = not applicable</i>	<i>(Generally matches CTD section title, but is restricted to 32 characters including 'period' and 3 character file extension if required - all lower case with underscore between words).</i>	<i>(Identifies universally acceptable file types plus additional, allowable file times)</i>	<i>(Comment to help guide the applicant in understanding the construction of the eCTD)</i>
			<i>n/a = not applicable Items in italics are examples and applicants may use the terminology they require so long as it adheres to the file naming conventions</i>		
Module 2	Common Technical Document Summaries	m2-common-technical-document-summaries	module_2	Folder name only	
2.1	Common Technical Document Table of Contents	n/a	n/a	Not required in eCTD	The 'Table of Contents' is created from the XML backbone description and the stylesheet applied
2.2	Introduction	m2-2-introduction	introduction.pdf	Single PDF file. In addition regional requirements may define RTF also.	
2.3	Quality Overall Summary	m2-3-quality-overall-summary	quality_overall_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	The Quality Overall Summary may be provided as a single PDF document or if the applicant wishes to subdivide the summary into constituent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.3.S	Introduction Drug Substance	m2-3-introduction m2-3-s-drug-substance	introduction_to_qos.pdf drug_substance	Folder name only	
2.3.S.1	General Information	m2-3-s-1-general-information	general_information.pdf		
2.3.S.2	Manufacture	m2-3-s-2-manufacture	manufacture.pdf		
2.3.S.3	Characterisation	m2-3-s-3-characterisation	characterization.pdf		
2.3.S.4	Control of Drug Substance	m2-3-s-4-control-of-drug-substance	control_drug_substance.pdf		
2.3.S.5	Reference Standards or Materials	m2-3-s-5-reference-standards-or-materials	reference_standards.pdf		

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.3.S.6	Container Closure System	m2-3-s-6-container-closure-system	container_closure_system.pdf		
2.3.S.7	Stability	m2-3-s-7-stability	stability.pdf		
2.3.P	Drug Product	m2-3-p-drug-product	drug_product	Folder name only	
2.3.P.1	Description and Composition of the Drug Product	m2-3-p-1-description-and-composition-of-the-drug-product	description_and_composition.pdf		
2.3.P.2	Pharmaceutical Development	m2-3-p-2-pharmaceutical-development	pharmaceutical_development.pdf		
2.3.P.3	Manufacture	m2-3-p-3-manufacture	manufacture.pdf		
2.3.P.4	Control of Excipients	m2-3-p-4-control-of-excipients	control_excipients.pdf		
2.3.P.5	Control of Drug Product	m2-3-p-5-control-of-drug-product	control_drug_product.pdf		
2.3.P.6	Reference Standards or Materials	m2-3-p-6-reference-standards-or-materials	reference_standards.pdf		
2.3.P.7	Container Closure System	m2-3-p-7-container-closure-system	container_closure_system.pdf		
2.3.P.8	Stability	m2-3-p-8-stability	stability.pdf		
2.3.A	Appendices	m2-3-a-appendices	appendices	Folder name only	
2.3.A.1	Facilities and Equipment	m2-3-a-1-facilities-and-equipment	facilities_and_equipment.pdf		
2.3.A.2	Adventitious Agents Safety Evaluation	m2-3-a-2-adventitious-agents-safety-evaluation	adventitious_agents.pdf		
2.3.A.3	Novel Excipients	m2-3-a-3-novel-excipients	novel_excipients	Folder name only	
2.3.R	Regional Information	m2-3-r-regional-information	regional_information	Folder name only	
2.4	Nonclinical Overview	m2-4-nonclinical-overview	nonclinical_overview.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	The Nonclinical Overview may be provided as a single PDF document or if the applicant wishes to subdivide the summary into constituent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.4.1	Overview of the Nonclinical Testing Strategy	m2-6-overview-of-the-nonclinical-testing-strategy	overview_testing_strategy.pdf		
2.4.2	Pharmacology	m2-4-2-pharmacology	pharmacology.pdf		
2.4.3	Pharmacokinetics	m2-4-3-pharmacokinetics	pharmacokinetics.pdf		
2.4.4	Toxicology	m2-4-4-toxicology	toxicology.pdf		
2.4.5	Integrated Overview and Conclusions	m2-4-5-integrated-overview-and-conclusion	integrated_overview.pdf		
2.4.6	List of Literature Citations	m2-4-6-list-of-literature-citations	references.pdf		

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.5	Clinical Overview	m2-5-clinical-overview	clinical_overview.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	The Clinical Overview may be provided as a single PDF document or if the applicant wishes to subdivide the summary into constituent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.5.1	Product Development Rationale	m2-5-1-product-development-rationale	product_develop_rationale.pdf		
2.5.2	Overview of Biopharmaceutics	m2-5-2-overview-of-biopharmaceutics	overview_biopharm.pdf		
2.5.3	Overview of Clinical Pharmacology	m2-5-3-overview-of-clinical-pharmacology	overview_clin_pharm.pdf		
2.5.4	Overview of Efficacy	m2-5-4-overview-of-efficacy	overview_efficacy.pdf		
2.5.5	Overview of Safety	m2-5-5-overview-of-safety	overview_safety.pdf		
2.5.6	Benefits and Risks Conclusions	m2-5-6-benefits-and-risks-conclusions	benefits_risks.pdf		
2.5.7	References	m2-5-7-references	references.pdf		
2.6	Nonclinical Written and Tabulated Summary	m2-6-nonclinical-written-and-tabulated-summary	nonclinical_summary	Folder name only	
2.6.1	Introduction	m2-6-1-introduction	introduction.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	
2.6.2	Pharmacology Written Summary	m2-6-2-pharmacology-written-summary	pharmacol_written_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This summary may be provided as a single PDF document or if the applicant wishes to subdivide the summary into constituent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.6.2.1	Brief Summary	m2-6-2-1-brief-summary	brief_summary.pdf		
2.6.2.2	Primary Pharmacodynamics	m2-6-2-2-primary-pharmacodynamics	primary_pharmacodynamics.pdf		
2.6.2.3	Secondary Pharmacodynamics	m2-6-2-3-secondary-pharmacodynamics	secondary_pharmacodynamics.pdf		
2.6.2.4	Safety Pharmacology	m2-6-2-4-safety-pharmacology	safety_pharmacology.pdf		
2.6.2.5	Pharmacodynamic Drug Interactions	m2-6-2-5-pharmacodynamic-drug-interactions	pd_drug_interactions.pdf		
2.6.2.6	Discussion and Conclusions	m2-6-2-6-discussion-and-conclusions	discussion_conclusions.pdf		
2.6.2.7	Tables and Figures	m2-6-2-7-tables-and-figures	tables_figures.pdf		Optional organisation for figures and tables

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.6.3	Pharmacology Tabulated Summary	m2-6-3-pharmacology-tabulated-summary	pharmacol_tabulated_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	Should have further navigation via bookmarks
2.6.4	Pharmacokinetics Written Summary	m2-6-4-pharmacokinetics-written-summary	pharmkin_written_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This summary may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.6.4.1	Brief Summary	m2-6-6-brief-summary	brief_summary.pdf		
2.6.4.2	Methods of Analysis	m2-6-4-2-methods-of-analysis	methods_analysis.pdf		
2.6.4.3	Absorption	m2-6-4-3-absorption	absorption.pdf		
2.6.4.4	Distribution	m2-6-4-4-distribution	distribution.pdf		
2.6.4.5	Metabolism (interspecies comparison)	m2-6-4-5-metabolism	metabolism.pdf		
2.6.4.6	Excretion	m2-6-4-6-excretion	excretion.pdf		
2.6.4.7	Pharmacokinetic Drug Interactions	m2-6-4-7-pharmacokinetic-drug-interactions	pk_drug_interactions.pdf		
2.6.4.8	Other Pharmacokinetic Studies	m2-6-4-8-other-pharmacokinetic-studies	other_pk_studies.pdf		
2.6.4.9	Discussion and Conclusions	m2-6-4-9-discussion-and-conclusions	discussion_conclusions.pdf		
2.6.4.10	Tables and Figures	m2-6-4-10-tables-and-figures	tables_figures.pdf		Optional organisation for figures and tables
2.6.5	Pharmacokinetics Tabulated Summary	m2-6-5-pharmacokinetics-tabulated-summary	pharmkin_tabulated_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	Should have further navigation via bookmarks
2.6.6	Toxicology Written Summary	m2-6-6-written-summary	toxicology_written_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This summary may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.6.6.1	Brief Summary	m2-6-6-1-brief-summary	brief_summary.pdf		
2.6.6.2	Single-Dose Toxicity	m2-6-6-2-single-dose-toxicity	single_dose_toxicity.pdf		

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.6.6.3	Repeat-Dose Toxicity (including supportive toxicokinetics evaluation)	m2-6-6-3-repeat-dose-toxicity	repeat_dose_toxicity.pdf		
2.6.6.4	Genotoxicity	m2-6-6-4-genotoxicity	genotoxicity.pdf		
2.6.6.5	Carcinogenicity (including supportive toxicokinetics evaluations)	m2-6-6-5-carcinogenicity	carcinogenicity.pdf		
2.6.6.6	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations)	m2-6-6-6-reproductive-and-development-toxicity	repro_develop_toxicity.pdf		
2.6.6.7	Local Tolerance	m2-6-6-7-local-tolerance	local_tolerance.pdf		
2.6.6.8	Other Toxicity Studies (if available)	m2-6-6-8-other-toxicity-studies	other_toxicity_studies.pdf		
2.6.6.9	Discussion and Conclusions	m2-6-6-9-discussion-and-conclusions	discussion_conclusions.pdf		
2.6.6.10	Tables and Figures	m2-6-6-10-tables-and-figures	tables_figures.pdf		Optional organisation for figures and tables
2.6.7	Toxicology Tabulated Summary	m2-6-7-toxicology-tabulated-summary	toxicology_tabulated_summary.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	Should have further navigation via bookmarks
2.7	Clinical Summary	m2-7-clinical-summary	clinical_summary	Folder name only	
2.7.1	Summary of Biopharmaceutic and Associated Analytical Methods	m2-7-1-summary-of-biopharmaceutic-and-associated-analytical-methods	summary_biopharm .pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This section may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so. If a single file, it should have further
2.7.1.1	Background and Overview	m2-7-1-1-background-and-overview	background_overview.pdf		
2.7.1.2	Summary of Results of Individual Studies	m2-7-1-2-summary-of-results-of-individual-studies	results_individual_studies.pdf		
2.7.1.3	Comparison and Analyses of Results Across Studies	m2-7-1-3-comparsion-and-analyses-of-results-across-studies	results_across_studies.pdf		
	Section 2.7.1 Appendix	m2-7-1-appendix	appendix_2_7_1.pdf		Optional organisation for figures and tables

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.7.2	Summary of Clinical Pharmacology Studies	m2-7-2-summary-of-clinical-pharmacology-studies	summary_clin_pharm.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This section may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so. If a single file, it should have further navigation via bookmarks
2.7.2.1	Background and Overview	m2-7-2-1-background-and-overview	background_overview.pdf		
2.7.2.2	Summary of Results of Individual Studies	m2-7-2-2-summary-of-results-of-individual-studies	results_individual_studies.pdf		
2.7.2.3	Comparison and Analyses of Results Across Studies	m2-7-2-3-comparison-and-analyses-of-results-across-studies	results_across_studies.pdf		
2.7.2.4	Special Studies	m2-7-2-4-special-studies	special_studies.pdf		
	Section 2.7.2 Appendix	m2-7-2-appendix	appendix_2_7_2.pdf		Optional organisation for figures and tables
2.7.3	Summary of Clinical Efficacy	m2-7-3-summary-of-clinical-efficacy	summary_clin_efficacy	Folder name only	When there is more than one drug substance, the name of the drug substance should be included in the file name (whilst remaining within the 32 character limit - and therefore may need to be abbreviated appropriately).
2.7.3.1	Background and Overview of Clinical Efficacy	m2-7-3-1-background-and-overview-of-clinical-efficacy	background_overview.pdf		
2.7.3.2	Summary of Results of Individual Studies	m2-7-3-2-summary-of-results-of-individual-studies	results_individual_studies.pdf		
2.7.3.3	Comparison and Analyses of Results Across Studies	m2-7-3-3-comparison-and-analyses-of-results-across-studies	results_across_studies.pdf		
2.7.3.3.1	Study Populations	m2-7-3-3-1-study-populations	study_populations.pdf		
2.7.3.3.2	Comparison of Efficacy Results of all Studies	m2-7-3-3-2-comparison-of-efficacy-results-of-all-studies	efficacy_all_studies.pdf		
2.7.3.3.3	Comparison of Results in Sub-Populations	m2-7-3-3-3-comparison-of-results-in-sub-populations	sub_populations.pdf		
2.7.3.4	Analysis of Clinical Information Relevant to Dosing Recommendations	m2-7-3-4-analysis-of-clinical-information-relevant-to-dosing-recommendations	clinical_info_dosing.pdf		
2.7.3.5	Persistence of Efficacy and/or Tolerance Effects	m2-7-3-5-persistence-of-efficacy-and-or-tolerance-effects	persistence_tolerance.pdf		
	Section 2.7.3. Appendix	m2-7-3-appendix	appendix_2_7_3.pdf		Optional organisation for figures and tables

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.7.4	Summary of Clinical Safety	m2-7-4-summary-of-clinical-safety	summary_clin_safety.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	This section may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so (but without the extension). If a single file, it should have further navigation via bookmarks
2.7.4.1	Exposure to the Drug	m2-7-4-1-exposure-to-the-drug	exposure_to_drug.pdf		
2.7.4.1.1	Overall Safety Evaluation Plan and Narratives of Safety Studies	m2-7-4-1-1-overall-safety-evaluation-plan-and-narratives-of-safety-studies	safety_plan_narratives.pdf		
2.7.4.1.2	Overall Extent of Exposure	m2-7-4-1-2-overall-extent-of-exposure	extent_exposure.pdf		
2.7.4.1.3	Demographic and Other Characteristics of Study Population	m2-7-4-1-3-demographic-and-other-characteristics-of-study-population	demograph_character.pdf		
2.7.4.2	Adverse Events	m2-7-4-2-adverse-events	adverse_events.pdf		
2.7.4.2.1	Analysis of Adverse Events	m2-7-4-2-1-analysis-of-adverse-events	analysis_adverse_events.pdf		
2.7.4.2.1.1	Common Adverse Events	m2-7-4-2-1-1-common-adverse-events	common_adverse_events.pdf		
2.7.4.2.1.2	Deaths	m2-7-4-2-1-2-deaths	deaths.pdf		
2.7.4.2.1.3	Other Serious Adverse Events	m2-7-4-2-1-3-other-serious-adverse-events	serious_adverse_events.pdf		
2.7.4.2.1.4	Other Significant Adverse Events	m2-7-4-2-1-4-other-significant-adverse-events	significant_adverse_events.pdf		
2.7.4.2.1.5	Analysis of Adverse Events by Organ System or Syndrome	m2-7-4-2-1-5-analysis-of-adverse-events-by-organ-system-or-syndrome	organ_system_syndrome.pdf		
2.7.4.2.2	Narratives	m2-7-4-2-2-narratives	narratives.pdf	PDF table with hyperlinks to narratives in Module 5	These narratives should already be located in the Clinical Study Reports in Module 5 and should not, therefore, be repeated in Module 2. It is sufficient to provide hyperlinks to the
2.7.4.3	Clinical Laboratory Evaluations	m2-7-4-3-clinical-laboratory-evaluations	clin_lab_evaluations.pdf		
2.7.4.4	Vital Signs, Physical Findings, and Other Observations Related to Safety	m2-7-4-4-vital-signs-physical-findings-and-other-observations-related-to-safety	observ_related_to_safety.pdf		
2.7.4.5	Safety in Special Groups and Situations	m2-7-4-5-safety-in-special-groups-and-situations	special_groups_situations.pdf		
2.7.4.5.1	Intrinsic Factors	m2-7-4-5-1-intrinsic-factors	intrinsic_factors.pdf		
2.7.4.5.2	Extrinsic Factors	m2-7-4-5-2-extrinsic-factors	extrinsic_factors.pdf		
2.7.4.5.3	Drug Interactions	m2-7-4-5-3-drug-interactions	drug_interactions.pdf		
2.7.4.5.4	Use in Pregnancy and Lactation	m2-7-4-5-4-use-in-pregnancy-and-lactation	pregnancy_lactation.pdf		

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
2.7.4.5.5	Overdose	m2-7-4-5-5-overdose	overdose.pdf		
2.7.4.5.6	Drug Abuse	m2-7-4-5-6-drug-abuse	drug_abuse.pdf		
2.7.4.5.7	Withdrawal and Rebound	m2-7-4-5-7-withdrawal-and-rebound	withdrawal_rebound.pdf		
2.7.4.5.8	Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability	m2-7-4-5-8-effects-on-ability-to-drive-or-operate-machinery-or-impairment-of-mental-ability	effects_ability.pdf		
2.7.4.6	Postmarketing Data	m2-7-4-6-postmarketing-data	post-marketing_data.pdf		
	Section 2.7.4 Appendix	m2-7-4-appendix	appendix_2_7_4.pdf		Optional organisation for figures and tables
2.7.5	References	m2-7-5-references	references.pdf	Single PDF file. In addition regional requirements may define RTF and XLS also.	
2.7.6	Synopses of Individual Studies	m2-7-6-synopses-of-individual-studies	synopses_indiv_studies.pdf	PDF table with hyperlinks to synopses in Module 5	These synopses should already be located in the Clinical Study Reports in Module 5 and should not, therefore, be repeated in Module 2. It is sufficient to provide hyperlinks to the locations in Module 5

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
		<i>(Uses CTD numbering scheme, always begins with a letter 'm' so as to meet XML standards for element names, uses lower case for consistency and uses hyphen throughout to avoid repeating 'periods') n/a = not applicable</i>	<i>(Generally matches CTD section title, but is restricted to 32 characters including 'period' and 3 character file extension if required - all lower case with underscore between words).</i>	<i>(Identifies universally acceptable file types plus additional, allowable file times)</i>	<i>(Comment to help guide the applicant in understanding the construction of the eCTD)</i>
	<i>Examples of specific files eg. study reports and references are identified using "...". and the cell highlighted in blue. Applicants should substitute these names for 'realistic' ones eg. the indication, a study number or the authors of a reference</i>		<i>n/a = not applicable Items in italics are examples and applicants may use the terminology they require so long as it adheres to the file naming conventions</i>		
Module 3	Quality	m3-quality	module_3	Folder name only	
3.1	Module 3 Table of Contents	n/a	n/a	Not required in eCTD	The 'Table of Contents' is created from the XML backbone description and the stylesheet applied
3.2	Body of Data	m3-2-body-of-data	body_of_data	Folder name only	
3.2.S	Drug Substance [Name of Substance]	m3-2-s-drug-substance	drug_substance	Folder name only	When there is more than one drug substance, the name of the drug substance should be included in the folder name (whilst remaining within the 32 character limit - and therefore may need to be abbreviated appropriately). Subsequent folders should be created for each drug substance included in the submission and the folder and file hierarchy beneath is repeated. Similarly, where there is more than one manufacturer, the drug substance folder should be repeated but with an indication of the manufacturer concerned included in the folder name. Again, the folder and file hierarchy beneath is repeated
3.2.S.1	General Information	m3-2-s-1-general-information	general_information	Folder name only	
3.2.S.1.1	Nomenclature	m3-2-s-1-1-nomenclature	nomenclature.pdf	Single PDF file	The principle in the Quality section would be to provide a single PDF file for each sub-section since this will facilitate the updating of sections as a whole allowing the agencies to more easily construct the 'current' file. The PDF file would have adequate bookmarking to provide further navigation
3.2.S.1.2	Structure	m3-2-s-1-2-structure	structure.pdf	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
3.2.S.1.3	General Properties	m3-2-s-1-3-general-properties	general_properties.pdf	Single PDF file	
3.2.S.2	Manufacture	m3-2-s-2-manufacture	manufacture	Folder name only	
3.2.S.2.1	Manufacturer(s)	m3-2-s-2-1-manufacturers	manufacturers.pdf	Single PDF file	
3.2.S.2.2	Description of Manufacturing Process and Process Controls	m3-2-s-2-2-description-of-manufacturing-process-and-process-controls	manuf_process_and_controls.pdf	Single PDF file for NCE, multiple PDF files for Biotech	
3.2.S.2.3	Control of Materials	m3-2-s-2-3-control-of-materials	control_of_materials.pdf	Single PDF file for NCE, multiple PDF files for Biotech	
3.2.S.2.4	Controls of Critical Steps and Intermediates	m3-2-s-2-4-controls-of-critical-steps-and-intermediates	control_critical_steps.pdf	Single PDF file	
3.2.S.2.5	Process Validation and/or Evaluation	m3-2-s-2-5-process-validation-and-or-evaluation	process_validation.pdf	Single PDF file for NCE, multiple PDF files for Biotech	
3.2.S.2.6	Manufacturing Process Development	m3-2-s-2-6-manufacturing-process-development	manuf_process_development.pdf	Single PDF file for NCE, multiple PDF files for Biotech	
3.2.S.3	Characterisation	m3-2-s-3-characterisation	characterisation	Folder name only	
3.2.S.3.1	Elucidation of Structure and Other Characteristics	m3-2-s-3-1-elucidation-of-structure-and-other-characteristics	elucidation_of_structure.pdf	Single PDF file	
3.2.S.3.2	Impurities	m3-2-s-3-2-impurities	impurities.pdf	Single PDF file	
3.2.S.4	Control of Drug Substance	m3-2-s-4-control-of-drug-substance	control_drug_substance	Folder name only	
3.2.S.4.1	Specification	m3-2-s-4-1-specification	specification.pdf	Single PDF file	
3.2.S.4.2	Analytical Procedures	m3-2-s-4-2-analytical-procedures	analytical_procedures.pdf	Single PDF file	
3.2.S.4.3	Validation of Analytical Procedures	m3-2-s-4-3-validation-of-analytical-procedures	validation_analyt_procedures.pdf	Single PDF file	
3.2.S.4.4	Batch Analyses	m3-2-s-4-4-batch-analyses	batch_analyses.pdf	Single PDF file	
3.2.S.4.5	Justification of Specification	m3-2-s-4-5-justification-of-specification	justification_of_specification.pdf	Single PDF file	
3.2.S.5	Reference Standards or Materials	m3-2-s-5-reference-standards-or-materials	reference_standards.pdf	Single PDF file	
3.2.S.6	Container Closure System	m3-2-s-6-container-closure-system	container_closure_system.pdf	Single PDF file	
3.2.S.7	Stability	m3-2-s-7-stability	stability	Folder name only	
3.2.S.7.1	Stability Summary and Conclusions	m3-2-s-7-1-stability-summary-conclusions	stability_summary.pdf	Single PDF file	
3.2.S.7.2	Post-approval Stability Protocol and Stability Commitment	m3-2-s-7-2-post-approval-stability-protocol-and-stability-commitment	postapproval_stability.pdf	Single PDF file	
3.2.S.7.3	Stability Data	m3-2-s-7-3-stability-data	stability_data.pdf	Single PDF file	
3.2.P	Drug Product	m3-2-p-drug-product	drug_product	Folder name only	Repeatable according to regional requirements only
3.2.P.1	Description and Composition of the Drug Product	m3-2-p-1-description-and-composition-of-the-drug-product	description_and_composition.pdf	Single PDF file	
3.2.P.2	Pharmaceutical Development	m3-2-p-2-pharmaceutical-development	pharmaceutical_development.pdf	Single PDF file.	This section may be provided as a single PDF document or if the applicant wishes to subdivide the summary into consistent parts they may choose to do so. The PDF file would have adequate bookmarking to provide further navigation

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
3.2.P.2.1	Components of the Drug Product	m3-2-p-2-1-components-of-the-drug-product	components_drug_product.pdf		
3.2.P.2.1.1	Drug Substance	m3-2-p-2-1-1-drug-substance	drug_substance.pdf		
3.2.P.2.1.2	Excipients	m3-2-p-2-1-2-excipients	excipients.pdf		
3.2.P.2.2	Drug Product	m3-2-p-2-2-drug-product	drug_product.pdf		
3.2.P.2.2.1	Formulation Development	m3-2-p-2-2-1-formulation-development	formulation_development.pdf		
3.2.P.2.2.2	Overages	m3-2-p-2-2-2-overages	overages.pdf		
3.2.P.2.2.3	Physicochemical and Biological Properties	m3-2-p-2-2-3-physicochemical-and-biologics-properties	physicochem_biolog_properties.pdf		
3.2.P.2.3	Manufacturing Process Development	m3-2-p-2-3-manufacturing-process-development	manuf_process_development.pdf		
3.2.P.2.4	Container Closure System	m3-2-p-2-4-container-closure-system	container_closure_system.pdf		
3.2.P.2.5	Microbiological Attributes	m3-2-p-2-5-microbiological-attributes	microbiological_attributes.pdf		
3.2.P.2.6	Compatibility	m3-2-p-2-6-compatibility	compatibility.pdf		
3.2.P.3	Manufacture	m3-2-p-3-manufacture	manufacture	Folder name only	
3.2.P.3.1	Manufacturer(s)	m3-2-p-3-1-manufacturers	manufacturers.pdf	Single PDF file	
3.2.P.3.2	Batch Formula	m3-2-p-3-2-batch-formula	batch_formula.pdf	Single PDF file	
3.2.P.3.3	Description of Manufacturing Process and Process Controls	m3-2-p-3-3-description-of-manufacturing-process-and-process-controls	manuf_process_and_controls.pdf	Single PDF file	
3.2.P.3.4	Controls of Critical Steps and Intermediates	m3-2-p-3-4-controls-of-critical-steps-and-intermediates	control_critical_steps.pdf	Single PDF file	
3.2.P.3.5	Process Validation and/or Evaluation	m3-2-p-3-5-process-validation-and-or-evaluation	process_validation.pdf	Single PDF file	
3.2.P.4	Control of Excipients	m3-2-p-4-control-of-excipients	control_excipients	Folder name only	
3.2.P.4.1	Specifications	m3-2-p-4-1-specifications	specifications.pdf	Single PDF file	
3.2.P.4.2	Analytical Procedures	m3-2-p-4-2-analytical-procedures	analytical_procedures.pdf	Single PDF file	
3.2.P.4.3	Validation of Analytical Procedures	m3-2-p-4-3-validation-of-analytical-procedures	validation_analyt_procedures.pdf	Single PDF file	
3.2.P.4.4	Justification of Specifications	m3-2-p-4-4-justification-of-specifications	justification_of_specification.pdf	Single PDF file	
3.2.P.4.5	Excipients of Human or Animal Origin	m3-2-p-4-5-excipients-of-human-or-animal-origin	excipients_human_animal.pdf	Single PDF file	
3.2.P.4.6	Novel Excipients	m3-2-p-4-6-novel-excipients	novel_excipients	Single PDF file	
3.2.P.5	Control of Drug Product	m3-2-p-5-control-of-drug-product	control_drug_product	Folder name only	
3.2.P.5.1	Specification(s)	m3-2-p-5-1-specifications	specifications.pdf	Single PDF file	
3.2.P.5.2	Analytical Procedures	m3-2-p-5-2-analytical-procedures	analytical_procedures.pdf	Single PDF file	
3.2.P.5.3	Validation of Analytical Procedures	m3-2-p-5-3-validation-of-analytical-procedures	validation_analyt_procedures.pdf	Single PDF file	
3.2.P.5.4	Batch Analyses	m3-2-p-5-4-batch-analyses	batch_analyses.pdf	Single PDF file	
3.2.P.5.5	Characterisation of Impurities	m3-2-p-5-5-characterisation-of-impurities	characterization_impurities.pdf	Single PDF file	
3.2.P.5.6	Justification of Specifications	m3-2-p-5-6-justification-of-specifications	justification_of_specification.pdf	Single PDF file	
3.2.P.6	Reference Standards or Materials	m3-2-p-6-reference-standards-or-materials	reference_standards.pdf	Single PDF file	
3.2.P.7	Container Closure System	m3-2-p-7-container-closure-system	container_closure_system.pdf	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
3.2.P.8	Stability	m3-2-p-8-stability	stability	Folder name only	
3.2.P.8.1	Stability Summary and Conclusion	m3-2-p-8-1-stability-summary-and-conclusion	stability_summary.pdf	Single PDF file	
3.2.P.8.2	Post-approval Stability Protocol and Stability Commitment	m3-2-p-8-2-post-approval-stability-protocol-and-stability-commitment	postapproval_stability.pdf	Single PDF file	
3.2.P.8.3	Stability Data	m3-2-p-8-3-stability-data	stability_data.pdf	Single PDF file	
3.2.A	Appendices	m3-2-a-appendices	appendices	Folder name only	
3.2.A.1	Facilities and Equipment	m3-2-a-1-facilities-and-equipment	facilities_and_equipment	Folder name only	Several reports are likely to be included in this appendix. The organisation is left to the applicant to define
	"Facilities and Equipment Report 1"		facilities_and_equipment_report_1.pdf	Single PDF file	
	"Facilities and Equipment Report 2"		facilities_and_equipment_report_2.pdf	Single PDF file	
	"Facilities and Equipment Report n"		facilities_and_equipment_report_n.pdf	Single PDF file	
3.2.A.2	Adventitious Agents Safety Evaluation	m3-2-a-2-adventitious-agents-safety-evaluation	adventitious_agents	Folder name only	For nonviral adventitious agents reports should be placed in this folder. For viral adventitious agents the following sub-folder structure should be used. An example of the file naming convention is given for each folder
	"Adventitious Agents Safety Evaluation Report 1"		adventitious_agents_1.pdf	Single PDF file	
	"Adventitious Agents Safety Evaluation Report 2"		adventitious_agents_2.pdf	Single PDF file	
	"Adventitious Agents Safety Evaluation Report n"		adventitious_agents_n.pdf	Single PDF file	
3.2.A.3	Novel Excipient [Name]	m3-2-a-3-novel-excipient	novel_excipient	Folder name only	Include the name of any novel excipient in the folder name. Insert a repeat of the drug substance section here for the novel excipient if the regional requirement define the need for such information to be included in the submission directly
3.2.R	Regional Information	m3-2-r-regional-information	regional_information	Folder name only	Refer to regional requirements
3.3	Literature References	m3-3-literature-references	references	Folder name only	
	"Reference 1"		reference_1.pdf	Single PDF file	An alternative approach is allowable whereby a single PDF file includes all references with bookmarks to each individual reference. However, this would mean that the whole file would need to be replaced if any update is made to its components
	"Reference 2"		reference_2.pdf	Single PDF file	
	"Reference n"		reference_n.pdf	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	<i>Examples of specific files eg. study reports and references are identified using "...". and the cell highlighted in blue. Applicants should substitute these names for 'realistic' ones eg. the indication, a study number or the authors of a reference</i>	<i>(Uses CTD numbering scheme, always begins with a letter 'm' so as to meet XML standards for element names, uses lower case for consistency and uses hyphen throughout to avoid repeating 'periods') n/a = not applicable</i>	<i>(Generally matches CTD section title, but is restricted to 32 characters including 'period' and 3 character file extension if required - all lower case with underscore between words).</i>	<i>(Identifies universally acceptable file types plus additional, allowable file times)</i>	<i>(Comment to help guide the applicant in understanding the construction of the eCTD)</i>
			<i>n/a = not applicable Items in italics are examples and applicants may use the terminology they require so long as it adheres to the file naming conventions</i>		
Module 4	Nonclinical Study Reports	m4-nonclinical-study-reports	module_4	Folder name only	
4.1	Table of Contents	n/a	n/a	Not required in eCTD	The 'Table of Contents' is created from the XML backbone description and the stylesheet applied
4.2	Study Reports	m4-2-study-reports	study_reports	Folder name only	
4.2.1	Pharmacology	m4-2-1-pharmacology	pharmacology	Folder name only	
4.2.1.1	Primary Pharmacodynamics	m4-2-1-1-primary-pharmacodynamics	primary_pharmacodynamics	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	Is possible to have the additional graphic file(s) inserted directly into the PDF file, thus making management of the file easier. Alternatively, the applicant may choose to manage these independently
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	The data listings may be included as part of the study report document or as a separate appendix. Regional requirements may allow the submission of the data listings as a data file. Refer to regional guidances

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.1.2	Secondary Pharmacodynamics	m4-2-1-2-secondary-pharmacodynamics	secondary_pharmacodynamics	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.1.3	Safety Pharmacology	m4-2-1-3-safety-pharmacology	safety_pharmacology	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.1.4	Pharmacodynamic Drug Interactions	m4-2-1-4-pharmacodynamics-drug-interactions	pd_drug_interactions	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2	Pharmacokinetics	m4-2-2-pharmacokinetics	pharmacokinetics	Folder name only	
4.2.2.1	Analytical Methods and Validation Reports (if separate reports are available)	m4-2-2-1-analytical-methods-and-validation-reports	analyt_methods_validation	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.2	Absorption	m4-2-2-2-absorption	absorption	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.3	Distribution	m4-2-2-3-distribution	distribution	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.4	Metabolism	m4-2-2-4-metabolism	metabolism	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.5	Excretion	m4-2-2-5-excretion	excretion	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.6	Pharmacokinetic Drug Interactions (nonclinical)	m4-2-2-6-pharmacokinetic-drug-interactions	pk_drug_interactions	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.2.7	Other Pharmacokinetic Studies	m4-2-2-7-other-pharmacokinetic-studies	other_pk_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3	Toxicology	m4-2-3-toxicology	toxicology	Folder name only	
4.2.3.1	Single-Dose Toxicity (in order by species, by route)	m4-2-3-1-single-dose-toxicity	single_dose_toxicity	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.2	Repeat-Dose Toxicity (in order by species, by route, by duration, including supportive toxicokinetics evaluations)	m4-2-3-2-repeat-dose-toxicity	repeat_dose_toxicity	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.3	Genotoxicity	m4-2-3-3-genotoxicity	genotoxicity	Folder name only	
4.2.3.3.1	In vitro	m4-2-3-3-1-in-vitro	in_vitro	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.3.2	In vivo (including supportive toxicokinetics evaluations)	m4-2-3-3-2-in-vivo	in_vivo	Folder name only	
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	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.4	Carcinogenicity (including supportive toxicokinetics evaluations)	m4-2-3-4-carcinogenicity	carcinogenicity	Folder name only	
4.2.3.4.1	Long-term studies (in order by species, including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)	m4-2-3-4-1-long-term-studies	long_term_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.4.2	Short- or medium-term studies (including range-finding studies that cannot be appropriately included under repeat-dose toxicity or pharmacokinetics)	m4-2-3-4-2-short-or-medium-term-studies	short_medium_term_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.4.3	Other studies	m4-2-3-4-3-other-studies	other_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.5	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations) (If modified study designs are used, the following subheadings should be modified accordingly.)	m4-2-3-5-reproductive-and-developmental-toxicity	repro_development_toxicity	Folder name only	
4.2.3.5.1	Fertility and early embryonic development	m4-2-3-5-1-fertility-and-early-embryonic-development	fertility_embryonic_develop	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.5.2	Embryo-fetal development	m4-2-3-5-2-embryo-fetal-development	embryo_fetal_develop	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.5.3	Prenatal and postnatal development, including maternal function	m4-2-3-5-3-prenatal-and-postnatal-development-including-maternal-function	pre_postnatal_develop	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.3.5.4	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated	m4-2-3-5-4-studies-in-which-the-offspring-juvenile-animals-are-dosed-and-or-further-evaluated	juvenile	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.4	Local Tolerance	m4-2-4-local-tolerance	local_tolerance	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5	Other Toxicity Studies (if available)	m4-2-5-other-toxicity-studies	other_toxicity_studies	Folder name only	
4.2.5.1	Antigenicity	m4-2-5-1-antigenicity	antigenicity	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5.2	Immunotoxicity	m4-2-5-2-immunotoxicity	immunotoxicity	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5.3	Mechanistic studies (if not included elsewhere)	m4-2-5-3-mechanistic-studies	mechanistic_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
4.2.5.4	Dependence	m4-2-5-4-dependence	dependence	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5.5	Metabolites	m4-2-5-5-metabolites	metabolites	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5.6	Impurities	m4-2-5-6-impurities	impurities	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.2.5.7	Other	m4-2-5-7-other	other	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 1 Data"		<i>study_report_1_data.pdf</i>	Single PDF file	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2 Data"		<i>study_report_2_data.pdf</i>	Single PDF file	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n Data"		<i>study_report_n_data.pdf</i>	Single PDF file	
4.3	Copies of Literature References	m4-3-copies-of-literature-references	references	Folder name only	
	"Reference 1"		<i>reference_1.pdf</i>	Single PDF file	An alternative approach is allowable whereby a single PDF file includes all references with bookmarks to each individual reference. However, this would mean that the whole file would need to be replaced if any update is made to its components
	"Reference 2"		<i>reference_2.pdf</i>	Single PDF file	
	"Reference n"		<i>reference_n.pdf</i>	Single PDF file	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	<i>Examples of specific files eg. study reports and references are identified using "...". and the cell highlighted in blue. Applicants should substitute these names for 'realistic' ones eg. the indication, a study number or the authors of a reference</i>	<i>(Uses CTD numbering scheme, always begins with a letter 'm' so as to meet XML standards for element names, uses lower case for consistency and uses hyphen throughout to avoid repeating 'periods') n/a = not applicable</i>	<i>(Generally matches CTD section title, but is restricted to 32 characters including 'period' and 3 character file extension if required - all lower case with underscore between words).</i>	<i>(Identifies universally acceptable file types plus additional, allowable file times)</i>	<i>(Comment to help guide the applicant in understanding the construction of the eCTD)</i>
			<i>n/a = not applicable Items in italics are examples and applicants may use the terminology they require so long as it adheres to the file naming conventions</i>		
Module 5	Clinical Study Reports	m5-clinical-study-reports	module_5	Folder name only	
5.1	Table of Contents for Study Reports	n/a	n/a	Not required in eCTD	The 'Table of Contents' is created from the XML backbone description and the stylesheet applied
5.2	Tabular Listing of all Clinical Studies	m5-2-tabular-listing-of-all-clinical-studies	tabular_listing.pdf	Single PDF file	
5.3	Clinical Study Reports	m5-3-clinical-study-reports	clinical_study_reports	Folder name only	
5.3.1	Reports of Biopharmaceutical Studies	m5-3-1-reports-of-biopharmaceutical-studies	biopharmaceutical_studies	Folder name only	
5.3.1.1	Bioavailability (BA) Study Reports	m5-3-1-1-bioavailability-ba-study-reports	bioavailability	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	It is possible to have the additional graphic file(s) inserted directly into the PDF file, thus making management of the file easier. Alternatively, the applicant may choose to manage these independently
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.1.2	Comparative BA and Bioequivalence (BE) Study Reports	m5-3-1-2-comparative-ba-and-bioequivalence-be-study-reports	comparative_ba_be	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
5.3.1.3	In vitro – In vivo Correlation Study Reports	m5-3-1-3-in-vitro-in-vivo-correlation-study-reports	in_vitro_in_vivo	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human Studies	m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-human-studies	bioanalyt_analyt_methods	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-human-biomaterials	pk_human_biomaterials	Folder name only	
5.3.2.1	Plasma Protein Binding Study Reports	m5-3-2-1-plasma-protein-binding-study-reports	plasma_protein_binding	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.2.2	Reports of Hepatic Metabolism and Interaction Studies	m5-3-2-2-reports-of-hepatic-metabolism-and-interaction-studies	hepatic_metab_interactions	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.2.3	Reports of Studies Using Other Human Biomaterials	m5-3-2-3-reports-of-studies-using-other-human-biomaterials	other_human_biomaterials	Folder name only	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.3	Reports of Human Pharmacokinetic (PK) Studies	m5-3-3-reports-of-human-pharmacokinetics-pk-studies	pk_studies	Folder name only	
5.3.3.1	Healthy Subject PK and Initial Tolerability Study Reports	m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-reports	healthy_subject_pk	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.3.2	Patient PK and Initial Tolerability Study Reports	m5-3-3-2-patient-pk-and-initial-tolerability-study-reports	patient_pk	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.3.3	Intrinsic Factor PK Study Reports	m5-3-3-3-intrinsic-factor-pk-study-reports	intrinsic_factor_pk	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		study_report_n.pdf	Single PDF file and exceptionally, additional graphics files	
5.3.3.4	Extrinsic Factor PK Study Reports	m5-3-3-4-extrinsic-factor-pk-study-reports	extrinsic_factor_pk	Folder name only	
	"Study Report 1"		study_report_1.pdf	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		study_report_2.pdf	Single PDF file and exceptionally, additional graphics files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.3.5	Population PK Study Reports	m5-3-3-5-population-pk-study-reports	population_pk	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.4	Reports of Human Pharmacodynamic (PD) Studies	m5-3-4-reports-of-human-pharmacodynamics-pd-studies	human_pd_studies	Folder name only	
5.3.4.1	Healthy Subject PD and PK/PD Study Reports	m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports	healthy_subject_pd	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.4.2	Patient PD and PK/PD Study Reports	m5-3-4-2-patient-pd-and-pk-pd-study-reports	patient_pd	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.5.	Reports of Efficacy and Safety Studies [indication]	m5-3-5-reports-of-efficacy-and-safety-studies	efficacy_safety	Folder name only	The name of the indication should be included in the folder name (whilst remaining within the 32 character limit - and therefore may need to be abbreviated appropriately). Subsequent folders should be created for each indication included in the submission and the folder and file hierarchy beneath is repeated.
5.3.5.1	Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	m5-3-5-1-study-reports-of-controlled-clinical-studies-pertinent-to-the-claimed-indication	controlled_studies	Folder name only	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.5.2	Study Reports of Uncontrolled Clinical Studies	m5-3-5-2-study-reports-of-uncontrolled-clinical-studies	uncontrolled_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.5.3	Reports of Analyses of Data from More than One Study	m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study	multistudy_analyses	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.5.4	Other Study Reports	m5-3-5-4-other-study-reports	other_studies	Folder name only	
	"Study Report 1"		<i>study_report_1.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report 2"		<i>study_report_2.pdf</i>	Single PDF file and exceptionally, additional graphics files	
	"Study Report n"		<i>study_report_n.pdf</i>	Single PDF file and exceptionally, additional graphics files	
5.3.6	Reports of Postmarketing Experience	m5-3-6-reports-of-postmarketing-experience	postmarketing_experience	Folder, but including either Single or Multiple PDF files	

CTD Numbering Scheme	CTD Section Title	eCTD DTD Element Name	Folder & File Names	File organisation	Comment for Applicant
5.3.7	Case Report Forms and Individual Patient Listings	m5-3-7-case-report-forms-and-individual-patient-listings	crfs_patient_listings	Folder name only	
	"Study 1"		study_1	Folder name only	
	"Document/Dataset 1"		document_dataset_1	As defined by regional requirements	
	"Document/Dataset 2"		document_dataset_2	As defined by regional requirements	
	"Document/Dataset n"		document_dataset_n	As defined by regional requirements	
	"Study 2"		study_2	Folder name only	
	"Document/Dataset 1"		document_dataset_1	As defined by regional requirements	
	"Document/Dataset 2"		document_dataset_2	As defined by regional requirements	
	"Document/Dataset n"		document_dataset_n	As defined by regional requirements	
	"Study n"		study_n	Folder name only	
	"Document/Dataset 1"		document_dataset_1	As defined by regional requirements	
	"Document/Dataset 2"		document_dataset_2	As defined by regional requirements	
	"Document/Dataset n"		document_dataset_n	As defined by regional requirements	
5.4	Literature References	m5-4-literature-references	references	Folder name only	
	"Reference 1"		reference_1.pdf	Single PDF file	An alternative approach is allowable whereby a single PDF file includes all references with bookmarks to each individual reference. However, this would mean that the whole file would need to be replaced if any update is made to its components
	"Reference 2"		reference_2.pdf	Single PDF file	
	"Reference n"		reference_n.pdf	Single PDF file	

## **Appendix 4 CTD Module 1 Administrative Information and Prescribing Information**

The name of the folder for this section should be *module\_1*. This module contains administrative information that is unique for each region. There will be local requirements for both the content and electronic content of module 1. The eCTD backbone was developed to allow the transfer of this regional information to be included in a regulatory dossier.

Regional guidance will provide the specific instructions on how to provide the administrative forms and detailed prescribing information. Please refer to this information and appendix 9 when preparing module 1.

## Appendix 5 CTD Module 2 Summaries

### ***Introduction***

Documents that are provided in module 2 should be formatted as defined by the ICH Common Technical Document. There should also be consistency in the way navigation aids are provided. Each report that is longer than five pages should have a table of contents. Within each document, bookmarks and hypertext links from the table of contents should be provided to all tables, figures, publications, and appendices.

Hypertext links should be provided throughout the body of these documents to aid efficient navigation to annotations, related sections, publications, appendices, tables, and figures that are not located on the same page. If a list of references is included at the end of a document, there should be hypertext links to the appropriate publication.

Documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is not available or where a signature is required.

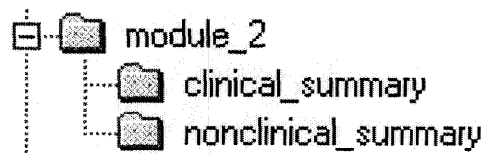
### ***Folder and File Naming Conventions for Module 2***

The name of the folder for module 2 should be *module\_2*. All folders that are created in the *module\_2* folder should follow the folder naming convention given in the following chapters. The folder hierarchy for module 2 is presented in the screenshot in Figure 1. This representation is by alphabetical order due to the nature of the operating system and is therefore not entirely consistent with the sequence of the CTD.

Several documents also reside in the module 2 folder. Although the file names for these documents are left to the discretion of the applicant, it is advisable to make the names meaningful unless there are other relevant factors to be considered. More details on the naming conventions are given in appendix 10 and examples in appendix 3.

The figure 5-1 shows the folder structure for module 2:

**Figure 5-1 Screenshot of the folder structure of module 2**



### ***Folders and files in Module 2***

Module 2 contains two folders, which should be named as follows.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
2.6	Nonclinical Written and Tabulated Summary	<i>nonclinical_summary</i>
2.7	Clinical Summary	<i>clinical_summary</i>

Other modules at this level not listed above may typically be submitted as individual files. However, the applicant may choose to submit more granular documents and if this is the case, detailed options are provided in appendix 3.

The two folders contain documents only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for module 2'.

## **Appendix 6 Module 3 Quality**

### ***Introduction***

Documents that are provided in module 3 should be formatted as defined by the ICH Common Technical Document. There should also be consistency in the way navigation aids are provided. Each report that is longer than five pages should have a table of contents. Within each document, bookmarks and hypertext links from the table of contents should be provided to all tables, figures, publications, and appendices.

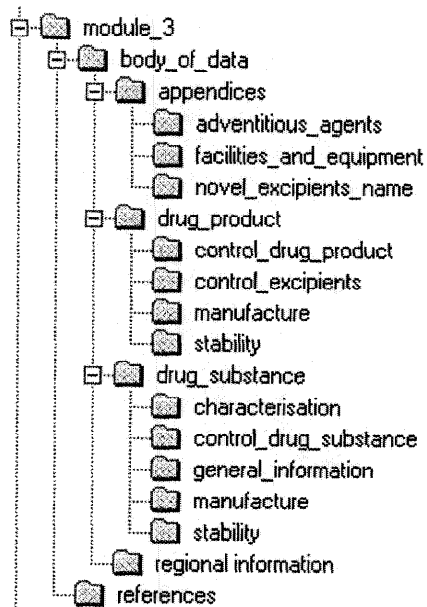
Hypertext links should be provided throughout the body of these documents to aid efficient navigation to annotations, related sections, publications, appendices, tables, and figures that are not located on the same page. If a list of references is included at the end of a document, there should be hypertext links to the appropriate publication.

Documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is not available or where a signature is required.

### ***Folder and File Naming Conventions for Module 3***

The name of the folder for module 3 should be *module\_3*. All folders that are created in the *module\_3* folder should follow the folder naming convention given in the following chapters. The full folder hierarchy for module 3 is presented in the screenshot in figure 6-1. This representation is by alphabetical order due to the nature of the operating system and is therefore not entirely consistent with the sequence of the CTD. All levels of the hierarchy should be used where information is available to include at that level.

**Figure 6-1 Folder structure of module 3**



### ***Folders and files in module 3***

Module 3 contains two folders, which should be named as follows. There are no files in Body of Data, there are files in Literature References.

Section in CTD	Description	Folder Name
3.2	Body of Data	<i>body_of_data</i>
3.3	Literature References	<i>references</i>

### ***Body of Data***

This folder may contain the following folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
S	Drug Substance <sup>1, 2</sup>	<i>drug_substance</i>
P	Drug Product <sup>3</sup>	<i>drug_product</i>
A	Appendices	<i>appendices</i>
R	Regional Information	<i>regional_information</i>

### ***Drug Substance***

This folder contains five folders, which should be named as follows.

Section in CTD	Description	Folder Name
3.2.S.1	General Information	<i>general_information</i>
3.2.S.2	Manufacture	<i>manufacture</i>
3.2.S.3	Characterisation	<i>characterisation</i>
3.2.S.4	Control of Drug Substance	<i>control_drug_substance</i>
3.2.S.7	Stability	<i>stability</i>

Other modules at this level not listed above may typically be submitted as individual files. Detailed options are provided in appendix 3.

<sup>1</sup> The folder name should include the name of the drug substance, abbreviated as necessary to remain with the 256 character limit. Folders and files should be created for each drug substance section included in the submission in accordance with the hierarchy identified in the following chapters.

<sup>2</sup> Similarly, if multiple manufacturers are used it may be appropriate to include the name of the manufacturer after the drug substance, abbreviated as necessary to remain with the 256 character limit. Folders and files should be created for each drug substance/manufacturer section included in the submission in accordance with the hierarchy identified in the following chapters.

<sup>3</sup> The folder name should include the name of the drug product, abbreviated as necessary to remain with the 256 character limit. Folders and files should be created for each drug product section included in the submission in accordance with the hierarchy identified in the following chapters. Reference should be made to regional guidance to determine whether the inclusion of multiple products within a single application is acceptable.

## ***Drug Product***

This folder contains four folders, which should be named as follows:

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
3.2.P.3	Manufacture	<i>manufacture</i>
3.2.P.4	Control of Excipients	<i>control_excipients</i>
3.2.P.5	Control of Drug Product	<i>control_drug_product</i>
3.2.P.8	Stability	<i>stability</i>

Other modules at this level not listed above may typically be submitted as individual files. Detailed options are provided in appendix 3.

## ***Appendices***

This folder contains three folders, which should be named as follows. There are no files in this folder.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
3.2.A.1	Facilities and Equipment	<i>facilities_and_equipment</i>
3.2.A.2	Adventitious Agents Safety Evaluation	<i>adventitious_agents</i>
3.2.A.3	Novel Excipient [name] <sup>4</sup>	<i>novel_excipient_name</i>

## ***Regional Information***

This folder should be included where regional information is necessary. Reference should be made to regional guidances for the types of information to be included in this section.

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<sup>4</sup> The folder name should include the name of the novel excipient, abbreviated as necessary to remain with the 256 character limit. Folders and files should be created as per the drug substance section in accordance with the hierarchy identified in the above chapters on drug substance for each novel excipient included.

## Appendix 7 Module 4 Nonclinical Study Reports

### *Introduction*

Documents that are provided in module 4 should be formatted as defined by the ICH Common Technical Document. There should also be consistency in the way navigation aids are provided. Each report that is longer than five pages should have a table of contents. Within each document, bookmarks and hypertext links from the table of contents should be provided to all tables, figures, publications, and appendices.

Hypertext links should be provided throughout the body of these documents to aid efficient navigation to annotations, related sections, publications, appendices, tables, and figures that are not located on the same page. If a list of references is included at the end of a document, there should be hypertext links to the appropriate publication.

Documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is not available or where a signature is required.

### *Folder and File Naming Conventions for Module 4*

The name of the folder for module 4 should be *module\_4*. All folders that are created in the *module\_4* folder should follow the folder naming convention given in the following chapters. The full folder hierarchy for module 4 is presented in the screenshot in Figure 7-1. This representation is by alphabetical order due to the nature of the operating system and is therefore not entirely consistent with the sequence of the CTD. It is not, however, mandatory to use the full folder hierarchy but in the case of this module, at least the first four levels should always be presented e.g. down to carcinogenicity and other folders at that level.

File names are left to the discretion of the applicant. In spite of this fact, it is advisable to make the names meaningful unless there are other relevant factors to be considered. Typically, the file name would be the internal numbering or naming convention for the studies. The following table gives an example how files could be named. In any case, file names should be written in small letters only and with underscores. More details on the naming conventions are given in appendix 10.

Description	File Name
Study Report 1	<i>study_report_1.pdf</i>
Study Report 2	<i>study_report_2.pdf</i>
...	...

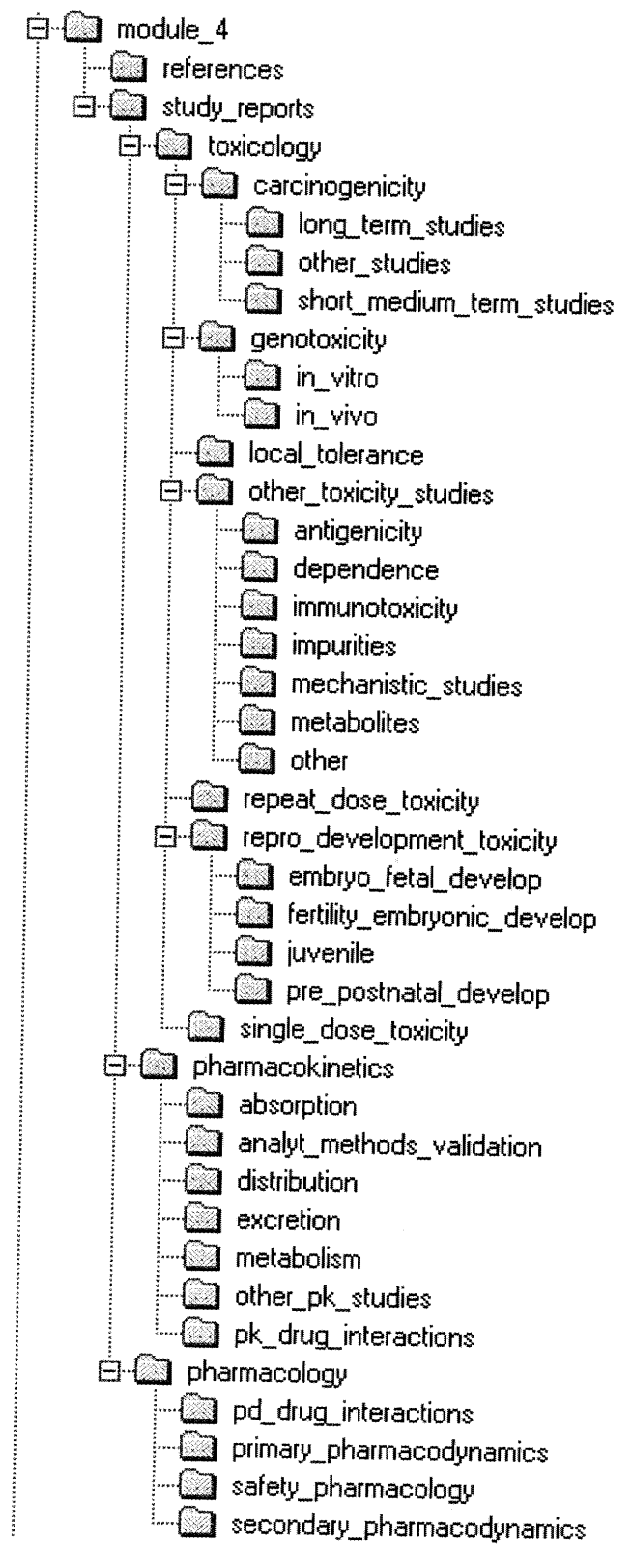
Study Report n	<i>study_report_n.pdf</i>
----------------	---------------------------

The data listings may be included as part of the study report document or as a separate appendix. If this approach is taken, the resulting file structure may be as follows.

<b>Description</b>	<b>File Name</b>
Study Report 1	<i>study_report_1.pdf</i>
Study Report 1 Data	<i>study_report_1_data.pdf</i>
Study Report 2	<i>study_report_2.pdf</i>
Study Report 2 Data	<i>study_report_2_data.pdf</i>
...	...
Study Report n	<i>study_report_n.pdf</i>
Study Report n Data	<i>study_report_n_data.pdf</i>

Regional requirements may allow the submission of the data listings as a data file. Reference should be made to regional guidances.

**Figure 7-1 Screenshot of the folder structure of module 4**



### ***Folders and files in module 4***

Module 4 contains two folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2	Study Reports	<i>study_reports</i>
4.3	Copies of Literature References	<i>references</i>

### ***Study Reports***

Study Reports contains five folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.1	Pharmacology	<i>pharmacology</i>
4.2.2	Pharmacokinetics	<i>pharmacokinetics</i>
4.2.3	Toxicology	<i>toxicology</i>
4.2.4	Local Tolerance	<i>local_tolerance</i>
4.2.5	Other Toxicity Studies (if available)	<i>other_studies</i>

The five folders contain reports or folders as outlined below. For the file naming convention see Section entitled 'Folder and File Naming Conventions for module 4'

### ***Pharmacology***

This folder contains four folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.1.1	Primary Pharmacodynamics	<i>primary_pharmacodynamics</i>
4.2.1.2	Secondary Pharmacodynamics	<i>secondary_pharmacodynamics</i>
4.2.1.3	Safety Pharmacology	<i>safety_pharmacology</i>
4.2.1.4	Pharmacodynamic Drug Interactions	<i>pd_drug_interactions</i>

The four folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

### ***Pharmacokinetics***

This folder contains seven folders, which should be named as follows. There are no files in this folder.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
4.2.2.1	Analytical Methods and Validation Reports (if separate reports are available)	<i>analyt_methods_validation</i>
4.2.2.2	Absorption	<i>absorption</i>
4.2.2.3	Distribution	<i>distribution</i>
4.2.2.4	Metabolism	<i>metabolism</i>
4.2.2.5	Excretion	<i>excretion</i>
4.2.2.6	Pharmacokinetic Drug Interactions (nonclinical)	<i>pk_drug_interactions</i>
4.2.2.7	Other Pharmacokinetic Studies	<i>other_pk_studies</i>

The seven folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

## ***Toxicology***

This folder contains five folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.3.1	Single-Dose Toxicity (in order by species, by route)	<i>single_dose_toxicity</i>
4.2.3.2	Repeat-Dose Toxicity (in order by species, by route, by duration, including supportive toxicokinetic evaluations)	<i>repeat_dose_toxicity</i>
4.2.3.3	Genotoxicity	<i>genotoxicity</i>
4.2.3.4	Carcinogenicity (including supportive toxicokinetics evaluations)	<i>carcinogenicity</i>
4.2.3.5	Reproductive and Developmental Toxicity (including range-finding studies and supportive toxicokinetics evaluations)	<i>repro_development_toxicity</i>

The two folders Single-Dose Toxicity and Repeat-Dose Toxicity contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

## ***Genotoxicity***

This folder contains two folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.3.3.1	In vitro	<i>in_vitro</i>
4.2.3.3.2	In vivo (including supportive toxicokinetics evaluations)	<i>in_vivo</i>

The two folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

## ***Carcinogenicity***

This folder contains three folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.3.4.1	Long-term studies (in order by species, including range-finding studies that cannot be appropriately include under repeat-dose toxicity or pharmacokinetics)	<i>long_term_studies</i>
4.2.3.4.2	Short-or medium-term studies (including range-finding studies that cannot be appropriately include under repeat-dose toxicity or pharmacokinetics)	<i>short_medium_term_studies</i>
4.2.3.4.3	Other studies	<i>other_studies</i>

The three folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

### ***Reproductive and Developmental Toxicity***

This folder contains four folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
4.2.3.5.1	Fertility and early embryonic development	<i>fertility_embryonic_develop</i>
4.2.3.5.2	Embryo-fetal development	<i>embryo_fetal_develop</i>
4.2.3.5.3	Prenatal and postnatal development, including maternal function	<i>pre_postnatal_develop</i>
4.2.3.5.4	Studies in which the offspring (juvenile animals) are dosed and/or further evaluated	<i>juvenile</i>

The four folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

### ***Local Tolerance***

This folder contains reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

### ***Other Toxicity Studies***

This folder contains seven folders, which should be named as follows. There are no files in this folder.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
4.2.5.1	Antigenicity	<i>antigenicity</i>
4.2.5.2	Immunotoxicity	<i>immunotoxicity</i>
4.2.5.3	Mechanistic studies (if not included elsewhere)	<i>mechanistic_studies</i>
4.2.5.4	Dependence	<i>dependence</i>
4.2.5.5	Metabolites	<i>metabolites</i>
4.2.5.6	Impurities	<i>impurities</i>
4.2.5.7	Other	<i>other</i>

The seven folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 4'.

## Appendix 8 Module 5 Clinical Study Reports

### *Introduction*

Documents that are provided in module 5 should be formatted as defined by the ICH Common Technical Document and by the ICH Guideline E3 – Structure and Content of Clinical Study Reports. There should also be consistency in the way navigation aids are provided. Each report that is longer than five pages should have a table of contents. Within each document, bookmarks and hypertext links from the table of contents should be provided to all tables, figures, publications, and appendices.

Hypertext links should be provided throughout the body of these documents to aid efficient navigation to annotations, related sections, publications, appendices, tables, and figures that are not located on the same page. If a list of references is included at the end of a document, there should be hypertext links to the appropriate publication.

Documents should be generated from electronic source documents and not from scanned material, except where access to the source electronic file is not available or where a signature is required.

### *Folder and File Naming Conventions for Module 5*

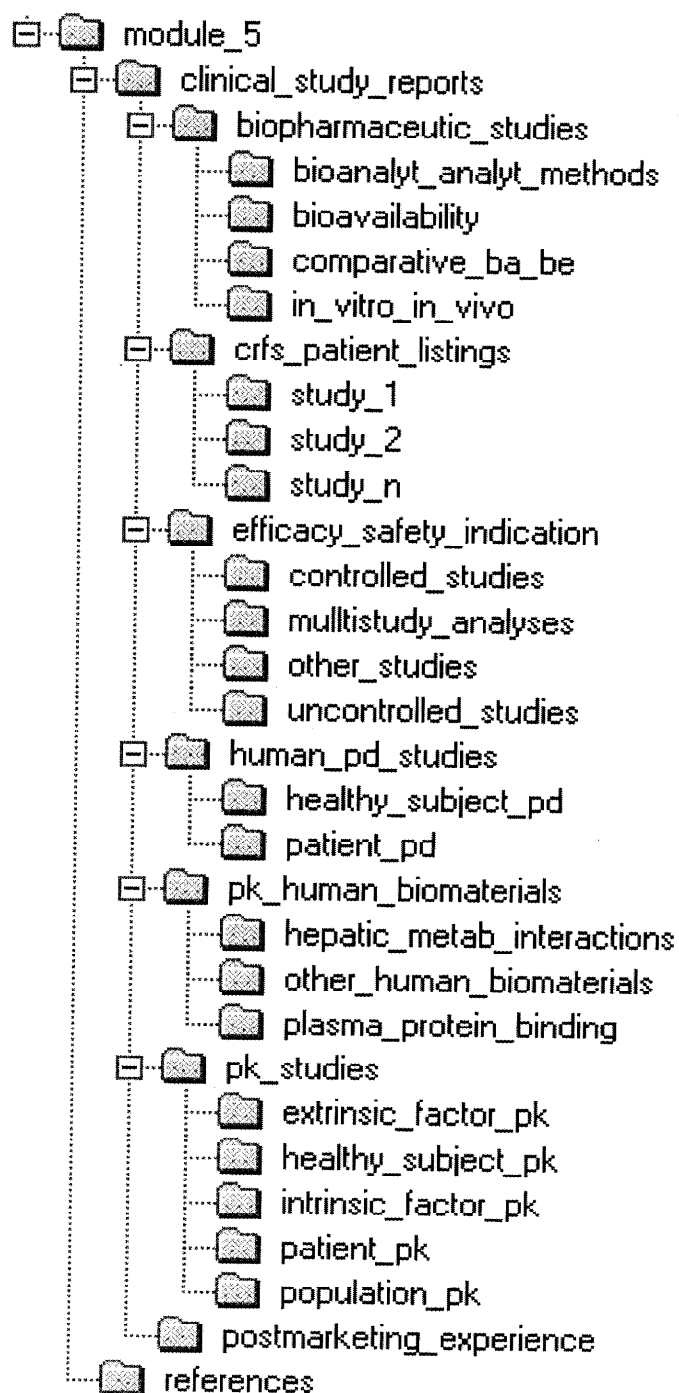
The name of the folder for module 5 should be *module\_5*. All folders that are created in the *module\_5* folder should follow the folder naming convention given in the following chapters. The full folder hierarchy for module 5 is presented in the screenshot in Figure 8-1. This representation is by alphabetical order due to the nature of the operating system and is therefore not entirely consistent with the sequence of the CTD. It is not, however, mandatory to use the full folder hierarchy but in the case of this module, at least the first three levels should always be presented e.g. down to *pk\_studies* and other folders at that level.

File names are left to the discretion of the applicant. In spite of this fact, it is advisable to make the names meaningful unless there are other relevant factors to be considered. Typically, the file name would be the internal numbering or naming convention for the studies. The following table gives an example how files could be named. In any case, file names should be written in small letters only and with underscores. More details on the naming conventions are given in appendix 10.

Description	File Name
Study Report 1	<i>study_report_1.pdf</i>
Study Report 2	<i>study_report_2.pdf</i>
...	...

Study Report n	<i>study_report_n.pdf</i>
----------------	---------------------------

**Figure 8-1 Screenshot of the folder structure of module 5**



### ***Folders and files in module 5***

Module 5 contains two folders, which should be named as follows.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
5.3	Clinical Study Reports	<i>clinical_study_reports</i>
5.4	References	<i>references</i>

Module 5 also contains one file. Although file names are left to the discretion of the applicant, it is advisable to make the names meaningful unless there are other relevant factors to be considered. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 5'

### ***Clinical Study Reports***

This folder contains seven folders, which should be named as follows. There are no files in this folder.

<b>Section in CTD</b>	<b>Description</b>	<b>Folder Name</b>
5.3.1	Reports of Biopharmaceutic Studies	<i>biopharmaceutic_studies</i>
5.3.2	Reports of Studies Pertinent to Pharmacokinetics using Human Biomaterials	<i>pk_human_biomaterials</i>
5.3.3	Reports of Human Pharmacokinetic (PK) Studies	<i>pk_studies</i>
5.3.4	Reports of Human Pharmacodynamic (PD) Studies	<i>human_pd_studies</i>
5.3.5	Reports of Efficacy and Safety Studies	<i>efficacy_safety_indication<sup>5</sup></i>
5.3.6	Reports of Postmarketing Experience	<i>postmarketing_experience</i>
5.3.7	Case Report Forms and Individual Patient Listings	<i>crfs_patient_listings</i>

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<sup>5</sup> The folder name should include the indication, abbreviated as necessary to remain with the 256 character limit. Subsequent folders should be created for each indication included in the submission and the folder and file hierarchy, identified in later chapters of this appendix is repeated

### ***Reports of Biopharmaceutic Studies***

This folder contains four folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
5.3.1.1	Bioavailability (BA) Study Reports	<i>bioavailability</i>
5.3.1.2	Comparative BA and Bioequivalence (BE) Study Reports	<i>comparative_ba_be</i>
5.3.1.3	In vitro – In vivo Correlation Study Reports	<i>in_vitro_in_vivo</i>
5.3.1.4	Reports of Bioanalytical and Analytical Methods for Human Studies	<i>bioanalyt_analyt_methods</i>

The four folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 5'.

### **REPORTS OF STUDIES PERTINENT TO PHARMACOKINETICS USING HUMAN BIOMATERIALS**

This folder contains three folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
5.3.2.1	Plasma Protein Binding Study Reports	<i>plasma_protein_binding</i>
5.3.2.2	Reports of Hepatic Metabolism and Interaction Studies	<i>hepatic_metab_interactions</i>
5.3.2.3	Reports of Studies Using Other Human Biomaterials	<i>other_human_biomaterials</i>

The three folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 5'.

### ***Reports of Human Pharmacokinetic (PK) Studies***

This folder contains five folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
5.3.3.1	Healthy Subject PK and Initial Tolerability Study Reports	<i>healthy_subject_pk</i>
5.3.3.2	Patient PK and Initial Tolerability Study Reports	<i>patient_pk</i>
5.3.3.3	Intrinsic Factor PK Study Reports	<i>intrinsic_factor_pk</i>
5.3.3.4	Extrinsic Factor PK Study Reports	<i>extrinsic_factor_pk</i>
5.3.3.5	Population PK Study Reports	<i>population_pk</i>

The five folders contain reports only. For the file naming convention see Section entitled 'Folder and File Naming Conventions for Module 5'.

### ***Reports of Human Pharmacodynamic (PD) Studies***

This folder contains two folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
5.3.4.1	Healthy Subject PD and PK/PD Study Reports	<i>healthy_subject_pd</i>
5.3.4.2	Patient PD and PK/PD Study Reports	<i>patient_pd</i>

The two folders contain reports only. For the file naming convention see Section entitled 'Folder and File Naming Conventions for Module 5'.

### ***Reports of Efficacy and Safety Studies***

This folder may be repeated as many times as pertinent to the number of indications claimed. Even when only one indication is applied for, the folder for this one indication should include the indication name. There are no files in this folder.

This folder contains four folders, which should be named as follows. There are no files in this folder.

Section in CTD	Description	Folder Name
5.3.5.1	Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication	<i>controlled_studies</i>
5.3.5.2	Study Reports of Uncontrolled Clinical Studies	<i>uncontrolled_studies</i>
5.3.5.3	Reports of Analyses of Data from More than One Study	<i>multistudy_analyses</i>
5.3.5.4	Other Study Reports	<i>other_studies</i>

The four folders contain reports only. For the file naming convention, see Section entitled 'Folder and File Naming Conventions for Module 5'

### ***Reports of Postmarketing Experience***

This folder contains reports only. File names should be meaningful and follow the file naming conventions given in appendix 10.

### ***Case Report Forms and Individual Patient Listings***

This folder contains as many folders as studies are included. The folders should be named as follows. The content of the folders should follow regional guidance.

Section in CTD	Description	Folder Name
5.3.7	"Study 1"	<i>study_1</i>
5.3.7	"Study 2"	<i>study_2</i>
...	...	...
5.3.7	"Study n"	<i>study_n</i>

## **Appendix 9 Region Specific Information Including Transmission and Receipt**

### ***Introduction***

This section describes region specific information: Content that is not explicitly included in the Common Technical Document and logistical details necessary for the transmission and receipt of submissions using the electronic Common Technical Document.

### ***Region specific information: Module 1***

Module 1 includes all administrative documents (e.g., forms and certifications) and labeling, including the documents described in regional guidance.

Module 1 contains regionally specific documents, but this does not mean that all regionally specific documents are included in module 1. Technical reports required for a specific region should be placed in modules 2 to 5. These reports should be included in the module most appropriate for the content of the information provided.

Each region provides specific guidance on the format and content of the regional requirements of each module. The Table 9-1 provides contact information for each region.

**Table 9-1**

<b>REGION</b>	<b>Internet Address</b>	<b>Electronic Mail Contact</b>
European Union	<a href="http://www.emea.eu.int">www.emea.eu.int</a>	<a href="mailto:Esubmission@emea.europa.org">Esubmission@emea.europa.org</a>
Food And Drug Administration, USA	<a href="http://www.fda.gov/cber">www.fda.gov/cber</a> <a href="http://www.fda.gov/cder">www.fda.gov/cder</a>	<a href="mailto:Esubprep@cber.fda.gov">Esubprep@cber.fda.gov</a> <a href="mailto:esub@cder.fda.gov">esub@cder.fda.gov</a>
Ministry of Health, Labor and Welfare, Japan	<a href="http://www.mhlw.go.jp">http://www.mhlw.go.jp</a> <a href="http://www.nihs.go.jp">http://www.nihs.go.jp</a>	
Health Canada		

### ***Submission Addresses***

Submissions should be sent directly to the appropriate national regulatory authority. Information necessary to send physical media to each regulatory authority is found at the reference location in Table 9-2.

**Table 9-2**

Regulatory Authority	Reference location
EMA, European Union Or national agencies	<a href="http://www.eudra.org/">http://www.eudra.org/</a> <a href="http://heads.medagencies.org">http://heads.medagencies.org</a>
Ministry of Health and Welfare, Japan	<a href="http://www.mhlw.go.jp">http://www.mhlw.go.jp</a> <a href="http://www.nihs.go.jp">http://www.nihs.go.jp</a>
Food and Drug Administration, United States of America	<a href="http://www.fda.gov/cder">http://www.fda.gov/cder</a> or <a href="http://www.fda.gov/cber">http://www.fda.gov/cber</a>
Health Canada, Health Protection Branch, Canada	<a href="http://www.hc-sc.gc.ca/hpb-dgps/therapeut">http://www.hc-sc.gc.ca/hpb-dgps/therapeut</a>

### **Media**

Regulatory authorities are prepared to accept electronic submissions provided on the media listed in Table 9-3. To optimize processing efficiency, we recommend choosing media with a capacity most appropriate to the size of the submission. Whenever possible, applicants should choose media capable of holding the submission on the fewest number of units. For example for a submission that has a size of 50 Megabytes, use 1 CD-ROM instead of 50 floppy disks.

**Table 9-3**

Recommendations for Media		Regulatory Authority
Example Size of Submission	MEDIA AND FORMAT	
Less than 10 MB	3.5 inch DOS Formatted Floppy Disks	EU, Japan*, USA, Canada
Less than 7 GB	CD-ROM ISO 9660	EU, Japan*, USA, Canada
Greater than 7 GB	Digital Tape – Compaq DLT 20/40 and 10/20 GB format using NT server 4.0 with NT backup or BackupExec	USA
	DVD	

\* MHLW: Except for module 1 originals.

### **Cover letter**

Provide a cover letter as a PDF file (cover.pdf). A paper cover letter should also be included with non-electronic portions of the submission (such as signed forms and certifications). The cover letter should include:

- A description of the submission including appropriate regulatory information.
- A listing of the sections of the submission filed as paper, electronic, or both paper and electronic.

- A description of the electronic submission including type and number of electronic media, approximate size of the submission, and, if appropriate, format used for DLT tapes.
- A statement that the submission is virus free with a description of the software used to check the files for viruses.
- The printed contents of the eCTD\_checksum.md5 file as an appendix.
- The regulatory and information technology points of contact for the submission.

### ***Preparing the media***

Send all electronic media adequately secured in a container marked clearly on the outside ELECTRONIC REGULATORY SUBMISSION. CD-ROMs should be packaged carefully to ensure that they arrive in a usable condition. Particularly vulnerable are diskettes and CD-ROM jewel cases shipped in envelopes without bubble-type protective material or stiff backing. The use of a jiffy-type bag by itself to ship media will not provide adequate protection for shipping electronic media. The first binder with electronic media should include only a paper copy of the cover letter for the submission, a paper copy of the appropriate regulatory authority form for the submission (e.g., for an NDA/BLA include FDA form 356h), and the electronic media for archiving. Please attach labels to the media including, for CD-ROMs, the CD-ROM jewel cases. Label the media with the following:

- Submission identifier (e.g., NDA, MAA number)
- Proprietary and generic name drug name.
- Company name
- Submission serial number, if applicable.
- Submission date: in the format of DD-MMM-YYYY (for example, 01-Jan-2001).
- Disk/CD-ROM/tape number (the number should include the total number submitted such as Disk # of #).
- Submission type (e.g., original submission, supplement, variation, etc.)

Regional specification:

MHLW:

- The Japanese year (the two digit Imperial year) may be accepted according to the regional requirement.
- Appended papers (documents) may also be included according to the regional requirement.

### ***Transport standards***

Secure EDI over the Internet is the recommended means for transporting submissions. However, until secure electronic gateways can be developed by the regulatory authorities, submissions will continue to be physically transported by courier or registered mail.

### ***Security standards***

Include an MD5 checksum for each physical file in the eCTD. The checksum allows the recipient to verify integrity of the physical files in the submission. The eCTD backbone DTD provides the location and tag names used for the checksums.

Include a checksum of the entire backbone instance. The recipient can use this checksum to ensure the integrity of the entire eCTD submission. Name this checksum file, eCTD\_checksum.md5 and include it as a file [on the first volume of the eCTD submission] in the same directory as the backbone instance. Print the contents of the eCTD\_checksum.md5 file and include the paper copy with the paper cover letter for the submission.

Do not include any file level security settings or password protection for individual files in the eCTD. Allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields. Internal security and access control processes in the regulatory authority will maintain the integrity of the submitted files.

### ***Receipt***

Upon arrival at the regulatory authority, the submission is copied (to tape for FDA/CDER, to the equivalent media for FDA/CBER and the EU). A read-only copy of the submission is then loaded onto the Electronic Document Room or equivalent server for use by the review community.

### ***Acknowledgment***

Each regulatory authority will acknowledge the receipt of the eCTD submission according to the policy and procedure of the individual regulatory authority. Use the address in Table 9-1 to find guidance on the format and content of acknowledgments.

## **Appendix 10 Preparation of the eCTD**

### ***Background***

There are many requirements that have influenced the design of the eCTD. Some that have had a more significant impact on the backbone design are:

- The submissions must accommodate full regulatory dossiers, supplements, amendments and variations.
- The submissions must be able to accommodate regional requirements that will be represented in regional guidance documents.
- The technology should be extensible so that as technology changes, the new electronic solutions can be accommodated.

The eCTD is designed around the concept of a Backbone. The Backbone is similar to a container that holds things like the submission name, the type of submission and the files that are part of the submission. The backbone is based on an XML Document Type Definition (DTD). There is a close relationship between the CTD table of contents and entities in the Backbone. The Backbone will provide the navigation links to the various files and information that make up the submission.

The folder names should be fixed names as defined in appendices 4 through 8. The highest-level folders should identify the submission using the submission number of the target regulatory authority and the next folder level should be named with the sequence number of that submission. The folders under the submission sequence number folder should follow the hierarchy of the table of contents of the submission. It is recommended that a limited number of files be located in a single folder, in order to facilitate user navigation through the submission. No empty folders should be included.

All file names must follow the naming conventions as defined in appendix 2 but the actual file names may be assigned by the sponsor of the submission.

In order to preserve the navigational linkages that are present in the documents contained in the eCTD, the directory structure will be preserved by the agencies. The navigational links will be relative links and links will be downward within a module.

The XML Backbone allows more than one entry or link to point to the same physical file. This should be done with caution since it may be more difficult for the regulatory authority to manage the life cycle of that file if there is more than one pointer to the file.

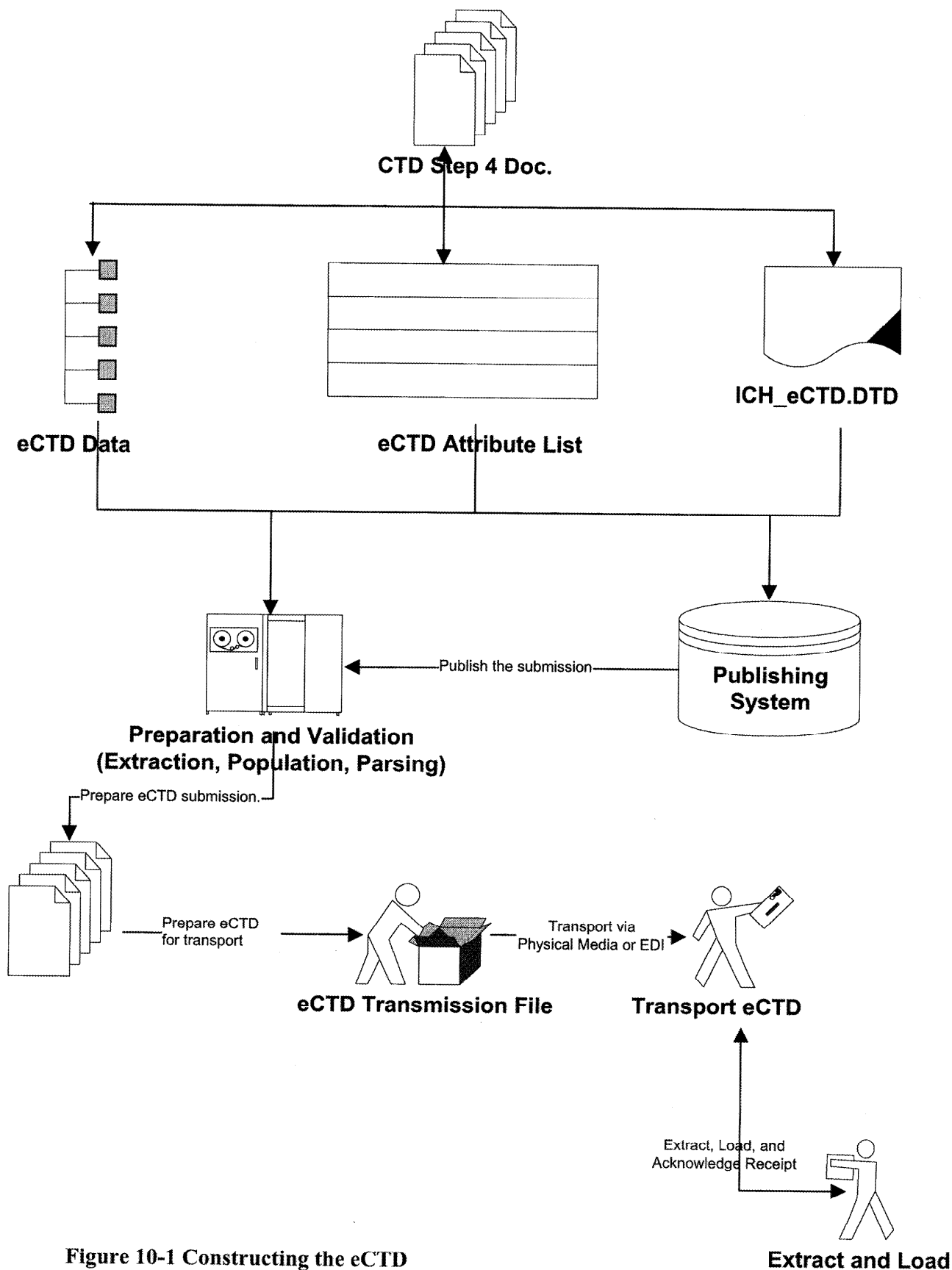
### ***Approach to Preparing the eCTD XML Data Files***

The M2 eCTD Specification includes the ICH eCTD DTD and a description of the elements and attributes list. The description and attribute list should be used to develop the eCTD instance that complies with the CTD document. The element and attribute description should be used in conjunction with the DTD to define the meaning of all of

the tags. This section is provided to help users understand the relationship between these products to develop a valid eCTD submission.

### ***Organization Required for Preparing eCTD XML Instances***

Using the ICH eCTD DTD to prepare eCTDs requires an organized approach and an understanding of the content and intended use of the ICH CTD document and the various M2 products. As shown in Figure 10-1, the process should begin with an in-depth study of the CTD document and the M2 eCTD Data Model and element and attribute description. One should be familiar with using XML version 1.0 as recommended by the W3C. Additional information can be found at the W3C web site at [www.w3c.org](http://www.w3c.org).



**Figure 10-1 Constructing the eCTD**

## Appendix 11 Creating the eCTD XML Submission

This appendix describes how to use the eCTD DTD to meet specific functional requirements. These functional requirements include:

- Intuitive user navigation at the folder and file level,
- Lifecycle management of submission files,
- File security,
- Population of the eCTD XML instance with files and metadata,
- Creation of complex relationships between files for submissions having multiple substances and products, or multiple indications, and
- Special needs for extending the DTD.

### *File Names and Directory Structure*

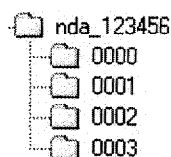
Recipients of the eCTD may need to directly navigate through the submission at the folder and file level, i.e.; without benefit of a customized end user application. The structure of the eCTD and instructions for how to create folder names facilitates this.

Specific folder names have been defined in appendices 4 through 8. File names are left to the discretion of the company. The top-level for the directory structure will vary by region. The identification of the top-level folder uniquely identifies the submission in a region. The submission identification should be used as the folder name in the top-level directory. For example, if the submission is number N123456, the root directory would be named "N123456". The original submission and subsequent amendments and variations should use the same top-level folder name. Submissions would be differentiated by a subfolder named according to the sequence number of the submission in that region. Submission identification number and sequence number will be submitted in regional DTDs as specified by each regulatory authority. Each regional DTD may be referenced in the eCTD DTD by the submitter. Table 11-1 and Figure 11-1 illustrate this naming convention, as it would apply in the United States.

**Table 11-1**

<b>Submission number</b>	<b>Sequence number</b>	<b>Type of submission</b>
N123456	0000	Original Submission
N123456	0001	First amendment, supplement or variation
N123456	0002	Second amendment, supplement or variation
...		
N123456	nnnn	Nth amendment, supplement or variation

**Figure 11-1**



## ***Lifecycle Management***

It is important for the recipients of eCTD to be able to establish where the submission fits in the lifecycle of a product.

The eCTD is capable of containing initial submissions, supplements, amendments and variations. There are no uniform definitions for these terms in the three regions, but amendments and supplements are terms used in the United States. Variations apply in Europe. The variations, supplements and amendments are used to provide additional information to an original regulatory dossier. For example, if a new formulation were being proposed, this would result in submission of an amendment or supplement to the FDA and a variation to Europe. When regulatory authorities request additional information, the information is also provided as a variation, supplement or amendment to the original submission. Therefore, the regulatory agencies need a way to manage the lifecycle for the submission. This function will be provided by each regulatory authority in the form guidance that may include regional DTDs and specifications. Each regional DTD should be referenced in the eCTD DTD by the submitter.

The eCTD DTD provides the for lifecycle management at the file level. When revisions are sent to a regulatory authority, the new file should be submitted as a leaf element associated with the same tag name as the file being amended or deleted. The “modified-file” attribute of the leaf element should contain the name and relative directory path of the file being amended, replaced or deleted. This will allow the regulatory authority to accurately locate the original file and update the original file’s status.

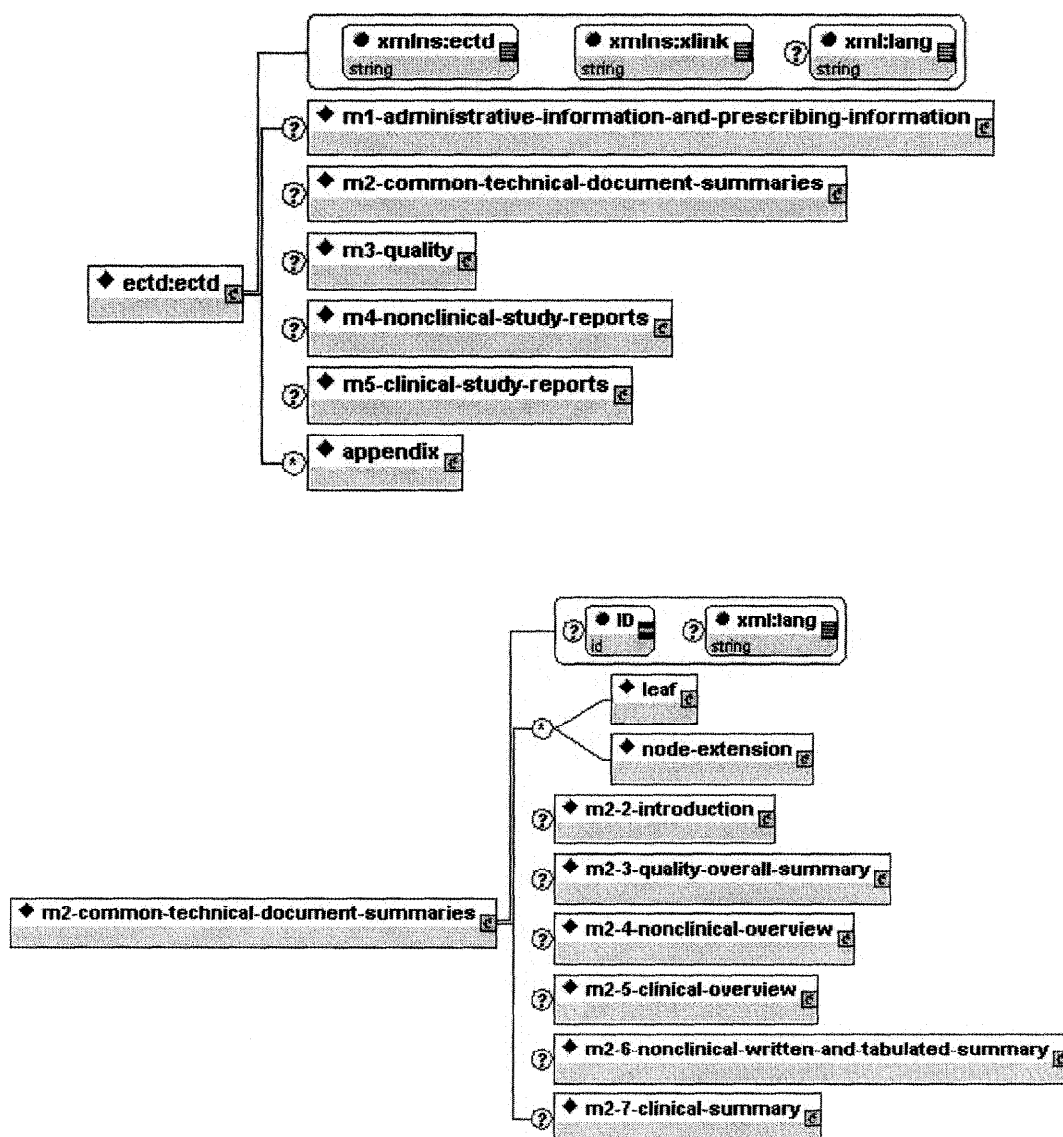
## ***Security***

A sponsor may provide the eCTD as an encrypted file in accordance with the ICH M2 Recommendation 4.1. This solution allows the eCTD to be encrypted and transferred over the Internet (if Internet receipt is implemented regionally) or to be encrypted on one of the approved physical media standards. The purpose of encryption is to protect the privacy of the confidential information and to insure it is only available to the authorized receiver. Encryption is always needed when the eCTD is sent via the Internet.

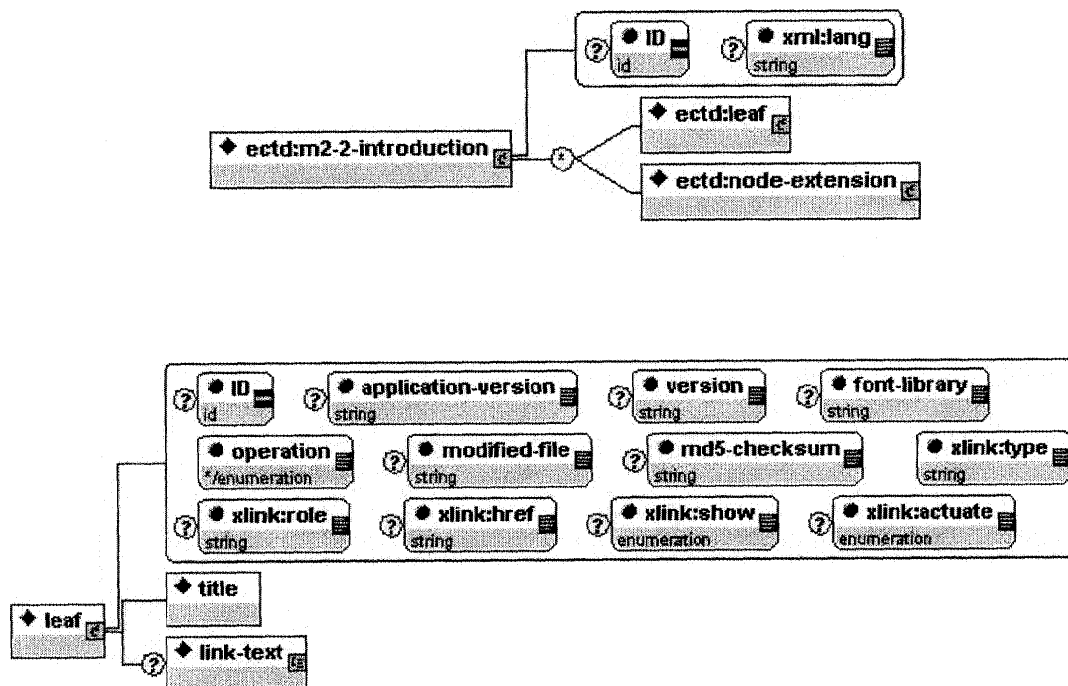
Encryption is not required if the information is sent using a physical media, although encryption is an option. The sponsor will assume all liability for the media until it is delivered to the regulatory authority.

### ***DTD Content Model***

The content model of the eCTD is derived from the organization of the Common Technical Document. The graphic representation of a portion of the content model is shown below. The content model is hierarchical starting at the “ectd” and going down to a specific item to be included in the submission. This example shows how the section containing technical document summaries is structured.



Once the appropriate tag has been selected, use the <leaf> element and attributes to specify a file in the submission. See “Instructions for preparing the eCTD” in this appendix for details.



## Instructions for preparing the eCTD

### FILES TO SUBMIT

For each submission the following files are expected:

- A valid eCTD.xml instance and the DTD.
- A valid regional XML instance and the DTD
- The MD5 checksum for the XML instance
- All files containing information that is part of the CTD.

The first five files listed above (eCTD.xml, the eCTD DTD, the regional XML file, the regional DTD and the MD5 checksum for the eCTD instance) should be submitted in the folder that identifies the submission sequence number. For example, for N123456 submission 0000, the files should be in N123456\0000.

The filename of the eCTD DTD, as distributed by the ICH, contains the version number of the DTD. This filename should not be changed and the file should be included in the submission. The DOCTYPE tag should include the filename of the DTD file:

```
<!DOCTYPE ectd:ectd SYSTEM "ectd_v091.dtd">
```

As shown in sample code fragment below, the eCTD.xml file should identify the regional XML file as a leaf in the element <m1- administrative-information-and-prescribing-information>.

```
<m1-administrative-information-and-prescribing-information>
  <leaf operation = "new" xlink:type = "simple" xlink:href =
    "fda_regional_0000.xml">
    <title>FDA regional 0000</title>
  </leaf>
</m1-administrative-information-and-prescribing-information>
```

### *eCTD Element/Attribute Instructions*

The eCTD consists of 6 primary sub modules:

- m1-administrative-information-and-prescribing-information
- m2-common-technical-document-summaries
- m3-quality
- m4-nonclinical-study-reports
- m5-clinical-study-reports
- Appendix

Each of the first 5 sub modules is further decomposed into sub-elements, each with a distinct <tag> that represents a CTD table of contents location. Complete the steps as shown in the following example all files being submitted for modules m1 through m5:

1. Select a tag element that best corresponds to the CTD table of contents location for a document or file being submitted. For example, select the tag <m2-4-2-pharmacology> to submit documents related to CTD to the overview of nonclinical summaries of pharmacology.
2. Create a child <leaf> element underneath the <m2-4-2-pharmacology> tag. If more than one file belongs at this level, you may create more than one <leaf> element under the tag.
3. Provide the relative location and file name of the actual file containing the overview of nonclinical summaries of pharmacology in the “xlink:href” attribute for the <leaf> element.
4. Provide a descriptive title for the file that contains the overview of nonclinical summaries of pharmacology in the <title> element of the <leaf>.
5. Provide information for the appropriate attributes of the <leaf> element as described in Table 11-2.

The following table describes each of these elements and attributes in further detail.

**Table 11-2**

Element	Attribute	Description/Instructions	Example
Any table of contents tag such as <m2-4-2-pharmacology>		<ul style="list-style-type: none"> <li>- A table of contents tag represents a grouping of one or more files related to a specific section of the Common Technical Document.</li> <li>- One or more child &lt;leaf&gt; elements may be declared for a parent table of contents tag.</li> <li>- A table of contents tag may be extended by providing a &lt;node-extension&gt; element under the table of contents tag. This is useful when information is being submitted that is more specific than specified by current tag names. However, you should only create a node extension at the lowest level of the existing table of contents. See the section “Instructions for extending eCTD tag elements” in this appendix.</li> </ul>	
	ID	A unique identifier for this location in the XML instance.	

Element	Attribute	Description/Instructions	Example
	xml:lang	The primary language used by the files in this entire section of the submission. Use ISO-639 standard language abbreviations	en
<leaf>		<ul style="list-style-type: none"> <li>- An leaf corresponds to a file.</li> <li>- One or more child leaf elements may be submitted for a parent table of contents tag.</li> </ul>	
	application-version	The version of the software application that was used to create this file.	Acrobat 4
	font-library	The commercial name of the font or font library needed to properly view the submitted file.	
	ID	Unique identifier for this location in the XML instance.	
	md5-checksum	The MD5 checksum for the file being submitted.	e854d3002c02a61fe5cbe926fd97b001
	modified-file	The name of the file to be modified as indicated in the “operation” attribute. This file name should include the relative path to the file. If no file is being modified, then do not supply the “modified-file” attribute.	\0000\module_2\clinical_summary\summaryintroduction.PDF
	operation	<p>Indicates the operation to be performed on the “modified-file”. Select one of the following valid values:</p> <p>new = the submitted file is new and there is no previously submitted file to perform an operation on.</p> <p>append = the new file has additional information that is to be reviewed with the previously submitted file.</p> <p>replace = the new file replaces the a previously submitted file.</p> <p>delete = indicates previously submitted file should no longer be used when reviewing the submission.</p>	new
	version	The file submittor’s internal version number or version identification for the report.	V23.5

Element	Attribute	Description/Instructions	Example
	xlink:actuate	Not Currently Used	
	xlink:href	Provide the pointer to the actual file. Use the relative path to the file and the file name.	module_2\clinical_summary\summaryintroduction.PDF
	xlink:role	Not Currently Used	
	xlink:show	Not Currently Used.	
	xlink:type	Fixed value of “simple”.	simple
<title>		Provide a description of the file being submitted.	<b>study report 1234</b>
	ID	Unique identifier for this location in the XML instance	1

### ***Instructions for a Simple New Submission***

The following XML fragment demonstrates the submission of a clinical overview of efficacy as a single PDF document.

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "ectd_v091.dtd">
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
  <m2-common-technical-document-summaries>
    <m2-5-clinical-overview>
      <m2-5-4-overview-of-efficacy xml:lang = "en">
        <leaf operation = "new" xlink:type = "simple" md5-checksum =
          "e854d3002c02a61fe5cbe926fd97b001"
          xlink:href = "module_2\clinical_summary\efficacy_overview.pdf"
          application-version = "Acrobat 5">
          <title>Overview of efficacy</title>
        </leaf>
      </m2-5-4-overview-of-efficacy>
    </m2-5-clinical-overview>
  </m2-common-technical-document-summaries>
</ectd:ectd>
```

This submission includes the file “efficacy\_overview.pdf” in the relative directory “module\_2\clinical\_summary” (i.e. the one starting below the Dossier number and submission sequence directories). The file is “new” and has a descriptive name of “Overview of efficacy”

The regional review application will treat this as a new submission to be associated with the submission identified in CTD module 1, which is region specific.

If this is the first submission for Dossier N123456, all the files in this submission are in the N123456\0000 directory or folder and below.

### ***Instructions for an Amendment, Supplement or Variation***

In the previous example, an efficacy overview was submitted. In this example, it is replaced by an updated version.

To replace a file, add the replacement file <leaf> element under the same tag element as the original file. If this is the second submission for Dossier N123456, all the files in this submission are in the N123456\0001 directory or folder and below.

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "ectd_v091.dtd">
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
  <m2-common-technical-document-summaries>
    <m2-5-clinical-overview>
      <m2-5-4-overview-of-efficacy xml:lang = "en">
        <leaf operation = "replace"
          xlink:type = "simple" md5-checksum =
            "e854d3002c02a61fe5cbe926fd973401"
          xlink:href = "module2\clinical_summary\efficacy_overview v2.pdf"
          application-version = "Acrobat 5"
          modified-file = "0000\module2\clinical_summary\efficacy_overview.pdf">
          <title>Overview of efficacy</title>
        </leaf>
      </m2-5-4-overview-of-efficacy>
    </m2-5-clinical-overview>
  </m2-common-technical-document-summaries>
</ectd:ectd>
```

### ***Instructions for Multiple Indications<sup>6</sup>***

Multiple therapeutic indications use an additional attribute associated with the <m2-7-3-summary-of-clinical-efficacy> and the <m5-3-5-reports-of-efficacy-and-safety-studies> elements to allow multiple indications to be submitted. The following table shows the use of these attributes.

**Table 11-3**

Element	Attribute	Description/Instructions	Example
<m2-7-3-summary-of-clinical-efficacy>	Indication	Name of the indication	pain
<m5-3-5-reports-of-efficacy-and-safety-studies>	Indication	Name of the indication.	pain

Note that the indication attribute is used by the regulatory authority to apply to all the table of contents tags beneath the <m2-7-3-summary-of-clinical-efficacy> and <m5-3-5-

<sup>6</sup> Note that these XML examples are examples only and do not necessarily contain all of the elements and attributes that you should use when preparing an eCTD submission.

reports-of-efficacy-and-safety-studies> tags. This is an example of the a section of the instance showing the submission of information about two indications:

```
<?xml version = "1.0" encoding = "UTF-8"?>
<!DOCTYPE ectd:ectd SYSTEM "ectd_v091.dtd">
<ectd:ectd xmlns:ectd = "http://www.ich.org/ectd" xmlns:xlink = "http://www.w3c.org/1999/xlink">
  <m2-common-technical-document-summaries>
    <m2-7-clinical-summary>
      <m2-7-3-summary-of-clinical-efficacy indication = "pain">
        <leaf operation = "new" xlink:type = "simple" xlink:href =
          "module_2\summary_clin_efficacy\pain_eff_sum.pdf">
          <title>pain efficacy summary</title>
        </leaf>
      </m2-7-3-summary-of-clinical-efficacy>
      <m2-7-3-summary-of-clinical-efficacy indication = "nausea">
        <leaf operation = "new" xlink:type = "simple" xlink:href =
          "module_2\summary_clin_efficacy\nausea_eff_sum.pdf">
          <title>nausea efficacy summary</title>
        </leaf>
      </m2-7-3-summary-of-clinical-efficacy>
    </m2-7-clinical-summary>
  </m2-common-technical-document-summaries>
  <m5-clinical-study-reports>
    <m5-3-clinical-study-reports>
      <m5-3-5-reports-of-efficacy-and-safety-studies indication = "pain">
        <leaf operation = "new" xlink:type = "simple" xlink:href =
          "module_5\clinical_study_reports\efficacy_safety_pain\pain_sr1.pdf">
          <title>pain study report 1</title>
        </leaf>
      </m5-3-5-reports-of-efficacy-and-safety-studies>
      <m5-3-5-reports-of-efficacy-and-safety-studies indication = "nausea">
        <leaf operation = "new" xlink:type = "simple" xlink:href =
          "module_5\clinical_study_reports\efficacy_safety_nausea\nausea_sr15.pdf">
          <title>nausea study report 15</title>
        </leaf>
      </m5-3-5-reports-of-efficacy-and-safety-studies>
    </m5-3-clinical-study-reports>
  </m5-clinical-study-reports>
</ectd:ectd>
```

### ***Instructions for Multiple Substances and Products***

Multiple drug substances use additional attributes associated with the <m3-2-s-drug-substance> element to allow unique combinations of the drug substance name and manufacturer to be submitted. The following table shows the use of these attributes.

**Table 11-4**

Element	Attribute	Description/Instructions	Example
<m3-2-s-drug-substance>	Substance	Name of one of the drug substances	Acetaminophen
	Manufacturer	Name of the manufacturer of the drug substance	my supplier

This is an example of the a section of the instance showing the submission of information about two drug substances, one of which is supplied by two manufacturers:

```
<m3-2-body-of-data>
  <m3-2-s-drug-substance substance = "acetaminophen" manufacturer = "my supplier">
    <leaf operation = "new" xlink:type = "simple" xlink:href =
      "module_3\body_of_data\drug_substance_acetaminophen2\acetaminophenMS.pdf">
      <title>acetaminophen / my supplier data</title>
    </leaf>
  </m3-2-s-drug-substance>
  <m3-2-s-drug-substance substance = "acetaminophen" manufacturer = "bulk company 2">
    <leaf operation = "new" xlink:type = "simple" xlink:href =
      "module_3\body_of_data\drug_substance_acetaminophen2\acetaminophen2.pdf">
      <title>acetaminophen / company 2 data</title>
    </leaf>
  </m3-2-s-drug-substance>
  <m3-2-s-drug-substance substance = "codeine" manufacturer = "drug company 2">
    <leaf operation = "new" xlink:type = "simple" xlink:href =
      "module_3\body_of_data\drug_substance_codeine\codeine_quality_data.pdf">
      <title>codeine data</title>
    </leaf>
  </m3-2-s-drug-substance>
</m3-2-body-of-data>
```

Multiple drug products use additional attributes associated with the < m3-2-p-drug-product> element to allow unique combinations of the drug product name and dosage form to be submitted. The following table shows the use of these attributes.

**Table 11-5**

Element	Attribute	Description/Instructions	Example
<m3-2-p-drug-product>	Product-name	Name of one of the drug products	Wonder drug
	Dosageform	Name of the dosage form of the drug product	Capsules

This is an example of a section of the instance showing the submission of information about two drug products:

```
<m3-2-body-of-data>
  <m3-2-p-drug-product product-name = "wonder drug" dosageform = "capsules">
    <leaf operation = "new" xlink:type = "simple" xlink:href =
      "module_3\body_of_data\drug_product_wonder_drug\specifications1.pdf">
      <title>wonder drug capsule product information</title>
    </leaf>
  </m3-2-p-drug-product>
  <m3-2-p-drug-product product-name = "wonder drug" dosageform = "tablets">
    <leaf operation = "new" xlink:type = "simple" xlink:href =
      "module_3\body_of_data\drug_product_wonder_drug\specifications2.pdf">
      <title>wonder drug tablet product information</title>
    </leaf>
  </m3-2-p-drug-product>
</m3-2-body-of-data>
```

```

<title>wonder drug tablet product data</title>
  </leaf>
</m3-2-p-drug-product>
</m3-2-body-of-data>

```

## ***Instructions for extending eCTD tag elements***

An applicant can extend the definition of an eCTD tag element by creating node extensions beneath a defined table of contents tag. The child element <node-extension> is required for each new table of contents node created. The <title> element value extends from the original eCTD tag name. You should follow the following principles when using <node-extension>:

1. Only extend the lowest level of defined eCTD tag names. For example you may extend the <m2-3-r-regional-information> tag but not the <m2-3-quality-overall-summary> tag since the latter is not the lowest tag defined in the table of contents.
2. Do not extend the eCTD tag name more than one level. For example, you should not extend <node-extension> <title>special-fda-summary</title> </node-extension> with another <node-extension>.

The following is an example of a section of the eCTD instance in which an applicant extends the <m2-3-r-regional-information> to provide specific regional information as requested by a regulatory authority. Alternatively, the regional information could have been provided as a <leaf> element under the <m2-3-r-regional-information> tag without the use of a “node extension”.

```

<m2-common-technical-document-summaries>
  <m2-3-quality-overall-summary>
    <m2-3-r-regional-information>
      <node-extension>
        <title>special-fda-summary</title>
        <leaf operation = "new" xlink:type = "simple" xlink:href =
          "module_2\quality_overall_summary\regional\fda\fda_extra_quality_sum.pdf">
          <title>regional quality summary required by the FDA</title>
        </leaf>
      </node-extension>
    </m2-3-r-regional-information>
  </m2-3-quality-overall-summary>
</m2-common-technical-document-summaries>

```

To update a file that has been submitted as an extended node, submit the replacement file using exactly the same eCTD tag and “node extension” information, including the <title> element for the <node-extension>. This makes it possible for the regulatory authority to locate the original file and update its status.

## **Appendix 12 Specification for PDF**

### ***INTRODUCTION***

This appendix describes the way in which PDF files should be constructed for inclusion in the eCTD. PDF is an open, published format created by Adobe Systems Incorporated (<http://www.adobe.com>). It is not necessary to use a product from Adobe or from any specific company to produce PDF documents. PDF is accepted as a standard for specific documents defined within Appendices x to x of this specification. The following recommendations will support the creation of PDF files that Agencies can review effectively. For any specification of Japanese version of PDF, please refer to the regional guidance.

### ***Version***

Agencies should be able to read all PDF files with version 4.0 of the Acrobat Reader with the search plug-in. Agencies should not need any additional software to read and navigate the PDF files. However, review will be facilitated through use of Acrobat Exchange version 4.0 since significantly more functionality is available in this product than with Acrobat Reader.

### ***Fonts***

#### **WESTERN CHARACTER SET**

PDF viewing software automatically substitutes a font to display text if the font used to create the text is unavailable on the reviewer's computer. Font substitution can affect a document's appearance and structure, and in some cases, it can affect the information conveyed by a document. Agencies cannot guarantee the availability of any fonts except those supported in the Acrobat product set itself that are Times New Roman, Arial and Courier. Therefore, all additional fonts used in the PDF files need to be embedded to ensure that those fonts will always be available to the reviewer. When embedding fonts, all characters for the font should be embedded, not just a subset of the fonts being used in the document.

One problem associated with embedding fonts is that embedding requires additional computer storage space. Three techniques to help limit the storage space taken by embedding fonts include:

- Limiting the number of fonts used in each document
- Using only True Type or Adobe Type 1 fonts
- Avoiding customised fonts

Resizing a document because the contents are too small to read is inefficient. Times New Roman, 12-point font, the font used for this document is adequate in size for reading narrative text and should be used whenever possible. It is sometimes tempting to use fonts which are smaller than 12 point in tables and charts but this should be avoided whenever possible. When choosing a point size for tables, a balance should be made

between providing sufficient information on a single page that may facilitate data comparisons for the reviewer while still achieving a point size that remains legible. The corollary of this is that in making point size larger, more tables may be necessary which may complicate data comparisons for a reviewer since data may now be included in separate tables. Generally, point sizes 9-10 are acceptable in tables but smaller point sizes should be avoided.

### ***Use of Coloured fonts***

The use of a black font colour is recommended. Blue font may be used for hypertext links. If a font colour other than black is used, avoid light colours that do not print well on greyscale printers. Colour reproduction can be tested prior to submission by printing sample pages from the document using a greyscale printer. The use of background shadowing should be avoided.

### ***Page Orientation***

Pages should be properly oriented so that all portrait pages are presented in portrait and all landscape pages are presented in landscape. To achieve this, the page orientation of landscape pages should be set to landscape prior to saving the PDF document in final form.

### ***Page Size and Margins***

The print area for pages should fit on a sheet of A4 or Letter paper. Overall margins should be sufficient and specifically, for pages in portrait orientation, a sufficient margin (at least 2.5cm) on the left side should be provided in order to avoid obscuring information if the reviewer subsequently prints and binds the pages for temporary use. For pages in landscape orientation (typically tables and publications) smaller margins are allowable (at least 2.0cm at the top and 0.8cm left and right) so as to allow more information, displayed legibly, on the page (see Section 3, Fonts). It is acceptable that header and footer information appears within these margins but not so close to the page edge that it may risk being lost upon printing.

### ***Source of Electronic Document***

PDF documents produced by scanning paper documents are usually inferior to those produced from an electronic source document. Scanned documents are more difficult to read and do not allow reviewers to search or copy and paste text for editing. They should be avoided where possible.

### ***Methods for Creating PDF Documents and Images***

The method used for creating PDF documents should produce the best replication of a paper document. To ensure that the paper and PDF version of the document are the same the document must be printed from the PDF version.

Documents that are available only in paper should be scanned at resolutions that will ensure the pages are legible both on the computer screen and when printed. At the same time, it is necessary to limit the file size. It is recommended that scanning is undertaken at a resolution of 300 dots per inch (dpi) to balance legibility and file size. The use of

greyscale or colour is discouraged because of file size. After scanning, avoid resampling to a lower resolution.

When creating PDF files containing images, the images should not be resampled.

Resampling does not preserve all of the pixels in the original. For PDF images, use one of the following lossless compression techniques:

- For lossless compression of colour and greyscale images, use Zip/Flate (one technique with two names). This is specified in Internet RFC 1950 and RFC 1951 (<http://info.internet.isi.edu/in-notes/rfc/files/rfc1950.txt>).
- For lossless compression of black and white images, use the CCITT Group 4 Fax compression technique. It is specified as CCITT recommendations T.6 (1988) - *Facsimile coding schemes and coding control functions for Group 4 facsimile apparatus*.

Paper documents containing hand-written notes should be scanned at 300 dpi. Hand-written notes should be done in black ink for clarity.

For photographs, the image should be obtained with a resolution of 600 dpi. If black and white photos are submitted, 8-bit grey scale images should be considered. If colour photos are submitted, 24-bit RGB images should be considered. A captured image should not be subjected to non-uniform scaling (i.e., sizing).

Gels and karyotypes should be scanned directly, rather than from photographs. Scanning should be at 600 dpi and 8-bit greyscale depth.

Plotter output graphics should be scanned or captured digitally at 300 dpi.

High-pressure liquid chromatography or similar images should be scanned at 300 dpi.

Applicants should validate the quality of the renditions with respect to the ability to handle satisfactorily and reliably the font sets of the European Union.

### ***Hypertext Linking and Bookmarks***

Hypertext links and bookmarks are techniques used to improve navigation through PDF documents. Hypertext links can be designated by rectangles using thin lines or by blue text.

In general, for documents with a table of contents, provide bookmarks for each item listed in the table of contents including all tables, figures, publications, other references, and appendices. These bookmarks are essential for the efficient navigation through documents. In general, including a bookmark to the main table of contents for a submission or item is helpful. The bookmark hierarchy should be made identical to the table of contents with no additional bookmark levels beyond those present in the table of contents.

Each additional level increases the need for space to read the bookmarks. The use of no more than 4 levels in the hierarchy is recommended.

Hypertext links throughout the body of the document to supporting annotations, related sections, references, appendices, tables, or figures that are not located on the same page are helpful and improve navigation efficiency. Relative paths must be used when

creating hypertext links to minimise the loss of hyperlink functionality when folders are moved between disk drives. Absolute links that reference specific drives and root directories will no longer work once the submission is loaded onto the Agency's network servers.

When creating bookmarks and hyperlinks, the magnification setting *Inherit Zoom* should be used so that the destination page displays at the same magnification level that the reviewer is using for the rest of the document.

### ***Page Numbering***

If a submission includes more than one document, no additional volume or page numbering is necessary. Only page numbers for individual documents are needed. It is easier to navigate through an electronic document if the page numbers for the document and the PDF file are the same. To accomplish this, the initial page of the paper document should be numbered page 1, with no use of Roman numerals or unnumbered pages in the document. If this is not done, Acrobat Reader would include such numbering within its page count and thus put the Acrobat numbering out of synchrony with the internal document page numbers.

Two exceptions to this rule may occur, details of which can be found in the guidances for the modules of the CTD.

- Firstly, where a document is split because of its size (eg. >50MB), under which circumstances the second or subsequent file would be numbered consecutively to that of the first or preceding file.
- Secondly, where several small documents with their own internal page numbering have been brought together into a single file, under which circumstances it is not necessary to provide additional page numbering but the start of each sub-document should be bookmarked.

### ***Document Information Fields***

Document information fields are used to search for individual documents and to identify the document when found. Recommendations for the document information fields will be provided in the guidance for the specific submission type.

### ***Open Dialog Box***

The open dialog box sets the document view when the file is opened. The initial view of the PDF files should be set as *Bookmarks* and *Page*. If there are no bookmarks, the initial view as *Page* only should be set. The *Magnification* and *Page Layout* should be set as default.

### ***Naming PDF Files***

Recommended names for folders and selected files will be provided in individual guidances for the modules.

When a file name is not specified, file names up to 256 characters in length with a 3-character extension can be used. The use of punctuation, spaces and other non-alphanumeric symbols in file names can be used, if necessary.

### ***Security***

No security settings or password protection for PDF files should be included. Security fields should be set to allow printing, changes to the document, selecting text and graphics, and adding or changing notes and form fields.

### ***Indexing PDF Documents***

Full text indices may be used to help find specific documents and/or search for text within documents. When a document or group of documents is indexed, all words and numbers in the file and all information stored in the Document Information fields are stored in special index files that are functionally accessible using the search tools available in Acrobat. Portions of a document that are imaged are not indexed. Even if the document only contains images, the text in the Document Information fields of the file will be indexed.

These full text indices should not be confused with a table of contents. Adobe Acrobat Catalog is one example of a tool that can be used to index PDF documents. Indices should not require extensions or additions to off-the-shelf Acrobat programs.

With many submissions, the table of contents file for a section should be associated with the corresponding full text index file. To associate means that once the table of contents file is opened, the index file is automatically added to the available index list and is ready to be used.

Further recommendations for full text indexes will be provided in guidances for the modules.

### ***Use of Acrobat Plug-Ins***

It is acceptable to use plug-ins to assist in the creation of a submission. However, the review of the submission should not require the use of any plug ins, in addition to those provided with Acrobat Exchange Version 4.0 because Agencies should not be required to archive additional plug-in functionality.

## Appendix 13 Specification for XML Files

XML was developed by a working group at the World Wide Web Consortium (W3C). It is a nonproprietary language developed to improve on previous mark up languages including standard generalized markup language (SGML) and hypertext markup language (HTML).

Information in an XML file is divided into specific pieces. These pieces are called objects or element types. The element type identifies the piece of information. For example, the name of the company submitting a marketing application in eCTD format for review is identified with the element type <applicant>. All element type names are bracketed using the special characters <>. Inside the XML document, the element type name is placed just prior to the piece of information and after the information. This is called tagging. So, in the XML file, the applicant could be tagged as follows <applicant>Worldwide Pharmaceuticals Inc.</applicant>. The / prior to the element type denotes that this is the end of the information about the applicant.

By using a hierarchical structure, XML allows you to relate two or more elements. This is accomplished by nesting one element within another.

Additional information about the element type is provided by attributes. Attributes are placed within the element types and are surrounded by “ ”. For example, if you wanted to show that the applicant name is presented in the English language, you could add this piece of information as an attribute. This could be represented in the XML file as <applicant XML:LANG=“EN”> Worldwide Pharmaceuticals Inc.</applicant>.

XML files are read by a parser found in internet browsers. Style sheets provide the browser with the information necessary to create tables, fonts, and colors for display.

The specific names of the element types and attributes as well as the valid syntax, structure and format for defining the XML elements are included in a file called document type declaration (DTD). If the XML document does not follow the DTD, then the file may not be able to be used properly.

At the beginning of the XML file, The top three lines of the XML file should include the XML version, the style sheet type and address, and the DTD name and address.

Additional information can be found at the W3C web site at [www.w3c.org](http://www.w3c.org).

## Appendix 14 eCTD Backbone DTD

```

<?xml version='1.0' encoding='UTF-8' ?>

<!-- eCTD Version 0.9 -->
<!-- ICH Tokyo Meeting: May 24, 2001 -->
<!-- eCTD Version 0.91 -->
<!-- June 4, 2001 -->
<!-- changed m2-7-3 to be 0 or more instead of 0 or 1 -->
<!ENTITY % att " ID ID #IMPLIED
    xml:lang CDATA #IMPLIED">

<!-- ===== -->
<!-- Top-level element -->
<!-- ===== -->
<!ELEMENT ectd:ectd (m1-administrative-information-and-prescribing-
information? , m2-common-technical-document-summaries? , m3-quality? ,
m4-nonclinical-study-reports? , m5-clinical-study-reports? , appendix*)>

<!ATTLIST ectd:ectd xmlns:ectd CDATA #FIXED 'http://www.ich.org/ectd'
    xmlns:xlink CDATA #FIXED
    'http://www.w3c.org/1999/xlink'
    xml:lang CDATA #IMPLIED >

<!-- ===== -->
<!-- Leaf content -->
<!-- ===== -->
<!ELEMENT leaf (title , link-text?)>

<!ATTLIST leaf ID ID #IMPLIED
    application-version CDATA #IMPLIED
    version CDATA #IMPLIED
    font-library CDATA #IMPLIED
    operation (new | append | replace | delete
) #REQUIRED
    modified-file CDATA #IMPLIED
    md5-checksum CDATA #IMPLIED
    xlink:type CDATA #FIXED 'simple'
    xlink:role CDATA #IMPLIED
    xlink:href CDATA #IMPLIED
    xlink:show (new | replace | embed | other |
none ) #IMPLIED
    xlink:actuate (onLoad | onRequest | other |
none ) #IMPLIED >
<!ELEMENT title (#PCDATA)>

<!ATTLIST title ID ID #IMPLIED >
<!ELEMENT link-text (#PCDATA | xref)*>

<!ATTLIST link-text ID ID #IMPLIED >
<!ELEMENT xref EMPTY>

<!ATTLIST xref ID ID #IMPLIED
    xlink:type CDATA #FIXED 'simple'
    xlink:role CDATA #IMPLIED
    xlink:title CDATA #REQUIRED
    xlink:href CDATA #REQUIRED

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                                xlink:show      (new | replace | embed | other | none )
#IMPLIED
                                xlink:actuate   (onLoad | onRequest | other | none )
#IMPLIED >
<!ELEMENT node-extension (title , (leaf | node-extension)+)>

<!ATTLIST node-extension  ID ID  #IMPLIED >
<!-- ===== -->
<!-- CTD Backbone structures -->
<!-- ===== -->
<!ELEMENT m1-administrative-information-and-prescribing-information
((leaf | node-extension)*)>

<!ATTLIST m1-administrative-information-and-prescribing-information
%att; >
<!ELEMENT m2-common-technical-document-summaries ((leaf | node-
extension)* , m2-2-introduction? , m2-3-quality-overall-summary? , m2-4-
nonclinical-overview? , m2-5-clinical-overview? , m2-6-nonclinical-
written-and-tabulated-summary? , m2-7-clinical-summary?)>

<!ATTLIST m2-common-technical-document-summaries %att; >
<!ELEMENT m2-2-introduction ((leaf | node-extension)*)>

<!ATTLIST m2-2-introduction %att; >
<!ELEMENT m2-3-quality-overall-summary ((leaf | node-extension)* , m2-3-
introduction? , m2-3-s-drug-substance? , m2-3-p-drug-product? , m2-3-a-
appendices? , m2-3-r-regional-information?)>

<!ATTLIST m2-3-quality-overall-summary %att; >
<!ELEMENT m2-3-introduction ((leaf | node-extension)*)>

<!ATTLIST m2-3-introduction %att; >
<!ELEMENT m2-3-s-drug-substance ((leaf | node-extension)* , m2-3-s-1-
general-information? , m2-3-s-2-manufacture? , m2-3-s-3-
characterisation? , m2-3-s-4-control-of-drug-substance? , m2-3-s-5-
reference-standards-or-materials? , m2-3-s-6-container-closure-system? ,
m2-3-s-7-stability?)>

<!ATTLIST m2-3-s-drug-substance %att; >
<!ELEMENT m2-3-s-1-general-information ((leaf | node-extension)*)>

<!ATTLIST m2-3-s-1-general-information %att; >
<!ELEMENT m2-3-s-2-manufacture ((leaf | node-extension)*)>

<!ATTLIST m2-3-s-2-manufacture %att; >
<!ELEMENT m2-3-s-3-characterisation ((leaf | node-extension)*)>

<!ATTLIST m2-3-s-3-characterisation %att; >
<!ELEMENT m2-3-s-4-control-of-drug-substance ((leaf | node-extension)*)>

<!ATTLIST m2-3-s-4-control-of-drug-substance %att; >
<!ELEMENT m2-3-s-5-reference-standards-or-materials ((leaf | node-
extension)*)>

<!ATTLIST m2-3-s-5-reference-standards-or-materials %att; >
<!ELEMENT m2-3-s-6-container-closure-system ((leaf | node-extension)*)>

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<!ATTLIST m2-3-s-6-container-closure-system %att; >
<!ELEMENT m2-3-s-7-stability ((leaf | node-extension)*)>

<!ATTLIST m2-3-s-7-stability %att; >
<!ELEMENT m2-3-p-drug-product ((leaf | node-extension)* , m2-3-p-1-
description-and-composition-of-the-drug-product? , m2-3-p-2-
pharmaceutical-development? , m2-3-p-3-manufacture? , m2-3-p-4-control-
of-excipients? , m2-3-p-5-control-of-drug-product? , m2-3-p-6-reference-
standards-or-materials? , m2-3-p-7-container-closure-system? , m2-3-p-8-
stability?)>

<!ATTLIST m2-3-p-drug-product %att; >
<!ELEMENT m2-3-p-1-description-and-composition-of-the-drug-product
((leaf | node-extension)*)>

<!ATTLIST m2-3-p-1-description-and-composition-of-the-drug-product
%att; >
<!ELEMENT m2-3-p-2-pharmaceutical-development ((leaf | node-
extension)*)>

<!ATTLIST m2-3-p-2-pharmaceutical-development %att; >
<!ELEMENT m2-3-p-3-manufacture ((leaf | node-extension)*)>

<!ATTLIST m2-3-p-3-manufacture %att; >
<!ELEMENT m2-3-p-4-control-of-excipients ((leaf | node-extension)*)>

<!ATTLIST m2-3-p-4-control-of-excipients %att; >
<!ELEMENT m2-3-p-5-control-of-drug-product ((leaf | node-extension)*)>

<!ATTLIST m2-3-p-5-control-of-drug-product %att; >
<!ELEMENT m2-3-p-6-reference-standards-or-materials ((leaf | node-
extension)*)>

<!ATTLIST m2-3-p-6-reference-standards-or-materials %att; >
<!ELEMENT m2-3-p-7-container-closure-system ((leaf | node-extension)*)>

<!ATTLIST m2-3-p-7-container-closure-system %att; >
<!ELEMENT m2-3-p-8-stability ((leaf | node-extension)*)>

<!ATTLIST m2-3-p-8-stability %att; >
<!ELEMENT m2-3-a-appendices ((leaf | node-extension)* , m2-3-a-1-
facilities-and-equipment? , m2-3-a-2-adventitious-agents-safety-
evaluation? , m2-3-a-3-novel-excipients?)>

<!ELEMENT m2-3-a-1-facilities-and-equipment ((leaf | node-extension)*)>

<!ATTLIST m2-3-a-1-facilities-and-equipment %att; >
<!ELEMENT m2-3-a-2-adventitious-agents-safety-evaluation ((leaf | node-
extension)*)>

<!ATTLIST m2-3-a-2-adventitious-agents-safety-evaluation %att; >
<!ELEMENT m2-3-a-3-novel-excipients ((leaf | node-extension)*)>

<!ATTLIST m2-3-a-3-novel-excipients %att; >
<!ELEMENT m2-3-r-regional-information ((leaf | node-extension)*)>

<!ATTLIST m2-3-r-regional-information %att; >

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<!ELEMENT m2-4-nonclinical-overview ((leaf | node-extension)* , m2-4-1-
overview-of-the-nonclinical-testing-strategy? , m2-4-2-pharmacology? ,
m2-4-3-pharmacokinetic? , m2-4-4-toxicology? , m2-4-5-integrated-
overview-and-conclusion? , m2-4-6-list-of-literature-citations?)>

<!ATTLIST m2-4-nonclinical-overview %att; >
<!ELEMENT m2-4-1-overview-of-the-nonclinical-testing-strategy ((leaf |
node-extension)*)>

<!ATTLIST m2-4-1-overview-of-the-nonclinical-testing-strategy %att; >
<!ELEMENT m2-4-2-pharmacology ((leaf | node-extension)*)>

<!ATTLIST m2-4-2-pharmacology %att; >
<!ELEMENT m2-4-3-pharmacokinetic ((leaf | node-extension)*)>

<!ATTLIST m2-4-3-pharmacokinetic %att; >
<!ELEMENT m2-4-4-toxicology ((leaf | node-extension)*)>

<!ATTLIST m2-4-4-toxicology %att; >
<!ELEMENT m2-4-5-integrated-overview-and-conclusion ((leaf | node-
extension)*)>

<!ATTLIST m2-4-5-integrated-overview-and-conclusion %att; >
<!ELEMENT m2-4-6-list-of-literature-citations ((leaf | node-
extension)*)>

<!ATTLIST m2-4-6-list-of-literature-citations %att; >
<!ELEMENT m2-5-clinical-overview ((leaf | node-extension)* , m2-5-1-
product-development-rationale? , m2-5-2-overview-of-biopharmaceutics? ,
m2-5-3-overview-of-clinical-pharmacology? , m2-5-4-overview-of-efficacy?
, m2-5-5-overview-of-safety? , m2-5-6-benefits-and-risks-conclusions? ,
m2-5-7-references?)>

<!ATTLIST m2-5-clinical-overview %att; >
<!ELEMENT m2-5-1-product-development-rationale ((leaf | node-
extension)*)>

<!ATTLIST m2-5-1-product-development-rationale %att; >
<!ELEMENT m2-5-2-overview-of-biopharmaceutics ((leaf | node-
extension)*)>

<!ATTLIST m2-5-2-overview-of-biopharmaceutics %att; >
<!ELEMENT m2-5-3-overview-of-clinical-pharmacology ((leaf | node-
extension)*)>

<!ATTLIST m2-5-3-overview-of-clinical-pharmacology %att; >
<!ELEMENT m2-5-4-overview-of-efficacy ((leaf | node-extension)*)>

<!ATTLIST m2-5-4-overview-of-efficacy %att; >
<!ELEMENT m2-5-5-overview-of-safety ((leaf | node-extension)*)>

<!ATTLIST m2-5-5-overview-of-safety %att; >
<!ELEMENT m2-5-6-benefits-and-risks-conclusions ((leaf | node-
extension)*)>

<!ATTLIST m2-5-6-benefits-and-risks-conclusions %att; >
<!ELEMENT m2-5-7-references ((leaf | node-extension)*)>

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<!ATTLIST m2-5-7-references %att; >
<!ELEMENT m2-6-nonclinical-written-and-tabulated-summary ((leaf | node-
extension)* , m2-6-1-introduction? , m2-6-2-pharmacology-written-
summary? , m2-6-3-pharmacology-tabulated-summary? , m2-6-4-
pharmacokinetics-written-summary? , m2-6-5-pharmacokinetics-tabulated-
summary? , m2-6-6-toxicology-written-summary? , m2-6-7-toxicology-
tabulated-summary?)>

<!ATTLIST m2-6-nonclinical-written-and-tabulated-summary %att; >
<!ELEMENT m2-6-1-introduction ((leaf | node-extension)*)>

<!ATTLIST m2-6-1-introduction %att; >
<!ELEMENT m2-6-2-pharmacology-written-summary ((leaf | node-extension)*
, m2-6-2-1-brief-summary? , m2-6-2-2-primary-pharmacodynamics? , m2-6-2-
3-secondary-pharmacodynamics? , m2-6-2-4-safety-pharmacology? , m2-6-2-
5-pharmacodynamic-drug-interactions? , m2-6-2-6-discussion-and-
conclusions? , m2-6-2-7-tables-and-figures?)>

<!ATTLIST m2-6-2-pharmacology-written-summary %att; >
<!ELEMENT m2-6-2-1-brief-summary ((leaf | node-extension)*)>

<!ATTLIST m2-6-2-1-brief-summary %att; >
<!ELEMENT m2-6-2-2-primary-pharmacodynamics ((leaf | node-extension)*)>

<!ATTLIST m2-6-2-2-primary-pharmacodynamics %att; >
<!ELEMENT m2-6-2-3-secondary-pharmacodynamics ((leaf | node-
extension)*)>

<!ATTLIST m2-6-2-3-secondary-pharmacodynamics %att; >
<!ELEMENT m2-6-2-4-safety-pharmacology ((leaf | node-extension)*)>

<!ATTLIST m2-6-2-4-safety-pharmacology %att; >
<!ELEMENT m2-6-2-5-pharmacodynamic-drug-interactions ((leaf | node-
extension)*)>

<!ATTLIST m2-6-2-5-pharmacodynamic-drug-interactions %att; >
<!ELEMENT m2-6-2-6-discussion-and-conclusions ((leaf | node-
extension)*)>

<!ATTLIST m2-6-2-6-discussion-and-conclusions %att; >
<!ELEMENT m2-6-2-7-tables-and-figures ((leaf | node-extension)*)>

<!ATTLIST m2-6-2-7-tables-and-figures %att; >
<!ELEMENT m2-6-3-pharmacology-tabulated-summary ((leaf | node-
extension)*)>

<!ATTLIST m2-6-3-pharmacology-tabulated-summary %att; >
<!ELEMENT m2-6-4-pharmacokinetics-written-summary ((leaf | node-
extension)* , m2-6-4-2-methods-of-analyses? , m2-6-4-3-absorption? , m2-
6-4-4-distribution? , m2-6-4-5-metabolism? , m2-6-4-6-excretion? , m2-6-
4-7-pharmacokinetic-drug-interactions? , m2-6-4-8-other-pharmacokinetic-
studies? , m2-6-4-9-discussion-and-conclusions? , m2-6-4-10-tables-and-
figures?)>

<!ATTLIST m2-6-4-pharmacokinetics-written-summary %att; >
<!ELEMENT m2-6-4-2-methods-of-analyses ((leaf | node-extension)*)>

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<!ATTLIST m2-6-4-2-methods-of-analyses %att; >
<!ELEMENT m2-6-4-3-absorption ((leaf | node-extension)*)>

<!ATTLIST m2-6-4-3-absorption %att; >
<!ELEMENT m2-6-4-4-distribution ((leaf | node-extension)*)>

<!ATTLIST m2-6-4-4-distribution %att; >
<!ELEMENT m2-6-4-5-metabolism ((leaf | node-extension)*)>

<!ATTLIST m2-6-4-5-metabolism %att; >
<!ELEMENT m2-6-4-6-excretion ((leaf | node-extension)*)>

<!ATTLIST m2-6-4-6-excretion %att; >
<!ELEMENT m2-6-4-7-pharmacokinetic-drug-interactions ((leaf | node-
extension)*)>

<!ATTLIST m2-6-4-7-pharmacokinetic-drug-interactions %att; >
<!ELEMENT m2-6-4-8-other-pharmacokinetic-studies ((leaf | node-
extension)*)>

<!ATTLIST m2-6-4-8-other-pharmacokinetic-studies %att; >
<!ELEMENT m2-6-4-9-discussion-and-conclusions ((leaf | node-
extension)*)>

<!ATTLIST m2-6-4-9-discussion-and-conclusions %att; >
<!ELEMENT m2-6-4-10-tables-and-figures ((leaf | node-extension)*)>

<!ATTLIST m2-6-4-10-tables-and-figures %att; >
<!ELEMENT m2-6-5-pharmacokinetics-tabulated-summary ((leaf | node-
extension)*)>

<!ATTLIST m2-6-5-pharmacokinetics-tabulated-summary %att; >
<!ELEMENT m2-6-6-toxicology-written-summary ((leaf | node-extension)* ,
m2-6-6-1-brief-summary? , m2-6-6-2-single-dose-toxicity? , m2-6-6-3-
repeat-dose-toxicity? , m2-6-6-4-genotoxicity? , m2-6-6-5-
carcinogenicity? , m2-6-6-6-reproductive-and-development-toxicity? , m2-
6-6-7-local-tolerance? , m2-6-6-8-other-toxicity-studies? , m2-6-6-9-
discussion-and-conclusions? , m2-6-6-10-tables-and-figures?)>

<!ATTLIST m2-6-6-toxicology-written-summary %att; >
<!ELEMENT m2-6-6-1-brief-summary ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-1-brief-summary %att; >
<!ELEMENT m2-6-6-2-single-dose-toxicity ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-2-single-dose-toxicity %att; >
<!ELEMENT m2-6-6-3-repeat-dose-toxicity ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-3-repeat-dose-toxicity %att; >
<!ELEMENT m2-6-6-4-genotoxicity ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-4-genotoxicity %att; >
<!ELEMENT m2-6-6-5-carcinogenicity ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-5-carcinogenicity %att; >

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<!ELEMENT m2-6-6-6-reproductive-and-development-toxicity ((leaf | node-
extension)*)>

<!ATTLIST m2-6-6-6-reproductive-and-development-toxicity %att; >
<!ELEMENT m2-6-6-7-local-tolerance ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-7-local-tolerance %att; >
<!ELEMENT m2-6-6-8-other-toxicity-studies ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-8-other-toxicity-studies %att; >
<!ELEMENT m2-6-6-9-discussion-and-conclusions ((leaf | node-
extension)*)>

<!ATTLIST m2-6-6-9-discussion-and-conclusions %att; >
<!ELEMENT m2-6-6-10-tables-and-figures ((leaf | node-extension)*)>

<!ATTLIST m2-6-6-10-tables-and-figures %att; >
<!ELEMENT m2-6-7-toxicology-tabulated-summary ((leaf | node-
extension)*)>

<!ATTLIST m2-6-7-toxicology-tabulated-summary %att; >
<!ELEMENT m2-7-clinical-summary ((leaf | node-extension)* , m2-7-1-
summary-of-biopharmaceutics-and-associated-analytical-methods? , m2-7-2-
summary-of-clinical-pharmacology-studies? , m2-7-3-summary-of-clinical-
efficacy* , m2-7-4-summary-of-clinical-safety? , m2-7-5-references? ,
m2-7-6-synopses-of-individual-studies?)>

<!ATTLIST m2-7-clinical-summary %att; >
<!ELEMENT m2-7-1-summary-of-biopharmaceutics-and-associated-analytical-
methods ((leaf | node-extension)* , m2-7-1-1-background-and-overview? ,
m2-7-1-2-summary-of-results-of-individual-studies? , m2-7-1-3-
comparsion-and-analyses-of-results-across-studies? , m2-7-1-4-
appendix?)>

<!ATTLIST m2-7-1-summary-of-biopharmaceutics-and-associated-analytical-
methods %att; >
<!ELEMENT m2-7-1-1-background-and-overview ((leaf | node-extension)*)>

<!ATTLIST m2-7-1-1-background-and-overview %att; >
<!ELEMENT m2-7-1-2-summary-of-results-of-individual-studies ((leaf |
node-extension)*)>

<!ATTLIST m2-7-1-2-summary-of-results-of-individual-studies %att; >
<!ELEMENT m2-7-1-3-comparsion-and-analyses-of-results-across-studies
((leaf | node-extension)*)>

<!ATTLIST m2-7-1-3-comparsion-and-analyses-of-results-across-studies
%att; >
<!ELEMENT m2-7-1-4-appendix ((leaf | node-extension)*)>

<!ATTLIST m2-7-1-4-appendix %att; >
<!ELEMENT m2-7-2-summary-of-clinical-pharmacology-studies ((leaf | node-
extension)* , m2-7-2-1-background-and-overview? , m2-7-2-2-summary-of-
results-of-individual-studies? , m2-7-2-3-comparision-and-analyses-of-
results-across-studies? , m2-7-2-4-special-studies? , m2-7-2-5-
appendix?)>

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<!ATTLIST m2-7-2-summary-of-clinical-pharmacology-studies %att; >
<!ELEMENT m2-7-2-1-background-and-overview ((leaf | node-extension)*)>

<!ATTLIST m2-7-2-1-background-and-overview %att; >
<!ELEMENT m2-7-2-2-summary-of-results-of-individual-studies ((leaf |
node-extension)*)>

<!ATTLIST m2-7-2-2-summary-of-results-of-individual-studies %att; >
<!ELEMENT m2-7-2-3-comparision-and-analyses-of-results-across-studies
((leaf | node-extension)*)>

<!ATTLIST m2-7-2-3-comparision-and-analyses-of-results-across-studies
%att; >
<!ELEMENT m2-7-2-4-special-studies ((leaf | node-extension)*)>

<!ATTLIST m2-7-2-4-special-studies %att; >
<!ELEMENT m2-7-2-5-appendix ((leaf | node-extension)*)>

<!ATTLIST m2-7-2-5-appendix %att; >
<!ELEMENT m2-7-3-summary-of-clinical-efficacy ((leaf | node-extension)*
, m2-7-3-1-background-and-overview-of-clinical-efficacy? , m2-7-3-2-
summary-of-results-of-individual-studies? , m2-7-3-3-comparision-and-
analyses-of-results-across-studies? , m2-7-3-4-analyses-of-clinical-
information-relevant-to-dosing-recommendations? , m2-7-3-5-persistence-
of-efficacy-and-or-tolerance-effects? , m2-7-3-6-appendix?)>

<!ATTLIST m2-7-3-summary-of-clinical-efficacy %att;
indication CDATA
#IMPLIED >
<!ELEMENT m2-7-3-1-background-and-overview-of-clinical-efficacy ((leaf |
node-extension)*)>

<!ATTLIST m2-7-3-1-background-and-overview-of-clinical-efficacy %att; >
<!ELEMENT m2-7-3-2-summary-of-results-of-individual-studies ((leaf |
node-extension)*)>

<!ATTLIST m2-7-3-2-summary-of-results-of-individual-studies %att; >
<!ELEMENT m2-7-3-3-comparision-and-analyses-of-results-across-studies
((leaf | node-extension)* , m2-7-3-3-1-study-populations? , m2-7-3-3-2-
comparison-of-efficacy-results-of-all-studies? , m2-7-3-3-3-comparison-
of-results-in-sub-populations?)>

<!ATTLIST m2-7-3-3-comparision-and-analyses-of-results-across-studies
%att; >
<!ELEMENT m2-7-3-3-1-study-populations ((leaf | node-extension)*)>

<!ATTLIST m2-7-3-3-1-study-populations %att; >
<!ELEMENT m2-7-3-3-2-comparison-of-efficacy-results-of-all-studies
((leaf | node-extension)*)>

<!ATTLIST m2-7-3-3-2-comparison-of-efficacy-results-of-all-studies
%att; >
<!ELEMENT m2-7-3-3-3-comparison-of-results-in-sub-populations ((leaf |
node-extension)*)>

<!ATTLIST m2-7-3-3-3-comparison-of-results-in-sub-populations %att; >

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<!ELEMENT m2-7-3-4-analyses-of-clinical-information-relevant-to-dosing-
recommendations ((leaf | node-extension)*)>

<!ATTLIST m2-7-3-4-analyses-of-clinical-information-relevant-to-dosing-
recommendations %att; >
<!ELEMENT m2-7-3-5-persistence-of-efficacy-and-or-tolerance-effects
((leaf | node-extension)*)>

<!ATTLIST m2-7-3-5-persistence-of-efficacy-and-or-tolerance-effects
%att; >
<!ELEMENT m2-7-3-6-appendix ((leaf | node-extension)*)>

<!ATTLIST m2-7-3-6-appendix %att; >
<!ELEMENT m2-7-4-summary-of-clinical-safety ((leaf | node-extension)* ,
m2-7-4-1-exposure-to-the-drug? , m2-7-4-2-adverse-events? , m2-7-4-3-
clinical-laboratory-evaluations? , m2-7-4-4-vital-signs-physical-
findings-and-other-observations-related-to-safety? , m2-7-4-5-safety-in-
special-groups-and-situations? , m2-7-4-6-post-marketing-data? , m2-7-4-
7-appendix?)>

<!ATTLIST m2-7-4-summary-of-clinical-safety %att; >
<!ELEMENT m2-7-4-1-exposure-to-the-drug ((leaf | node-extension)* , m2-
7-4-1-1-overall-safety-evaluation-plan-and-narratives-of-safety-studies?
, m2-7-4-1-2-overall-extent-of-exposure? , m2-7-4-1-3-demographic-and-
other-characteristics-of-study-population?)>

<!ATTLIST m2-7-4-1-exposure-to-the-drug %att; >
<!ELEMENT m2-7-4-1-1-overall-safety-evaluation-plan-and-narratives-of-
safety-studies ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-1-1-overall-safety-evaluation-plan-and-narratives-of-
safety-studies %att; >
<!ELEMENT m2-7-4-1-2-overall-extent-of-exposure ((leaf | node-
extension)*)>

<!ATTLIST m2-7-4-1-2-overall-extent-of-exposure %att; >
<!ELEMENT m2-7-4-1-3-demographic-and-other-characteristics-of-study-
population ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-1-3-demographic-and-other-characteristics-of-study-
population %att; >
<!ELEMENT m2-7-4-2-adverse-events ((leaf | node-extension)* , m2-7-4-2-
1-analysis-of-adverse-events? , m2-7-4-2-2-narratives)>

<!ATTLIST m2-7-4-2-adverse-events %att; >
<!ELEMENT m2-7-4-2-1-analysis-of-adverse-events ((leaf | node-
extension)* , m2-7-4-2-1-1-common-adverse-events? , m2-7-4-2-1-2-deaths?
, m2-7-4-2-1-3-other-serious-adverse-events? , m2-7-4-2-1-4-other-
significant-adverse-events? , m2-7-4-2-1-5-analysis-of-adverse-events-
by-organ-system-or-syndrome?)>

<!ATTLIST m2-7-4-2-1-analysis-of-adverse-events %att; >
<!ELEMENT m2-7-4-2-1-1-common-adverse-events ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-2-1-1-common-adverse-events %att; >
<!ELEMENT m2-7-4-2-1-2-deaths ((leaf | node-extension)*)>

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<!ATTLIST m2-7-4-2-1-2-deaths %att; >
<!ELEMENT m2-7-4-2-1-3-other-serious-adverse-events ((leaf | node-
extension)*)>

<!ATTLIST m2-7-4-2-1-3-other-serious-adverse-events %att; >
<!ELEMENT m2-7-4-2-1-4-other-significant-adverse-events ((leaf | node-
extension)*)>

<!ATTLIST m2-7-4-2-1-4-other-significant-adverse-events %att; >
<!ELEMENT m2-7-4-2-1-5-analysis-of-adverse-events-by-organ-system-or-
syndrome ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-2-1-5-analysis-of-adverse-events-by-organ-system-or-
syndrome %att; >
<!ELEMENT m2-7-4-2-2-narratives ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-2-2-narratives %att; >
<!ELEMENT m2-7-4-3-clinical-laboratory-evaluations ((leaf | node-
extension)*)>

<!ATTLIST m2-7-4-3-clinical-laboratory-evaluations %att; >
<!ELEMENT m2-7-4-4-vital-signs-physical-findings-and-other-observations-
related-to-safety ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-4-vital-signs-physical-findings-and-other-observations-
related-to-safety %att; >
<!ELEMENT m2-7-4-5-safety-in-special-groups-and-situations ((leaf |
node-extension)* , m2-7-4-5-1-intrinsic-factors? , m2-7-4-5-2-extrinsic-
factors? , m2-7-4-5-3-drug-interactions? , m2-7-4-5-4-use-in-pregnancy-
and-lactation? , m2-7-4-5-5-overdose? , m2-7-4-5-6-drug-abuse? , m2-7-
4-5-7-withdrawal-and-rebound? , m2-7-4-5-8-effects-on-ability-to-drive-
or-operate-machinery-or-impairment-of-mental-ability?)>

<!ATTLIST m2-7-4-5-safety-in-special-groups-and-situations %att; >
<!ELEMENT m2-7-4-5-1-intrinsic-factors ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-1-intrinsic-factors %att; >
<!ELEMENT m2-7-4-5-2-extrinsic-factors ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-2-extrinsic-factors %att; >
<!ELEMENT m2-7-4-5-3-drug-interactions ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-3-drug-interactions %att; >
<!ELEMENT m2-7-4-5-4-use-in-pregnancy-and-lactation ((leaf | node-
extension)*)>

<!ELEMENT m2-7-4-5-5-overdose ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-5-overdose %att; >
<!ELEMENT m2-7-4-5-6-drug-abuse ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-6-drug-abuse %att; >
<!ELEMENT m2-7-4-5-7-withdrawal-and-rebound ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-5-7-withdrawal-and-rebound %att; >
<!ELEMENT m2-7-4-5-8-effects-on-ability-to-drive-or-operate-machinery-
or-impairment-of-mental-ability ((leaf | node-extension)*)>

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<!ATTLIST m2-7-4-5-8-effects-on-ability-to-drive-or-operate-machinery-
or-impairment-of-mental-ability %att; >
<!ELEMENT m2-7-4-6-post-marketing-data ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-6-post-marketing-data %att; >
<!ELEMENT m2-7-4-7-appendix ((leaf | node-extension)*)>

<!ATTLIST m2-7-4-7-appendix %att; >
<!ELEMENT m2-7-5-references ((leaf | node-extension)*)>

<!ATTLIST m2-7-5-references %att; >
<!ELEMENT m2-7-6-synopses-of-individual-studies ((leaf | node-
extension)*)>

<!ATTLIST m2-7-6-synopses-of-individual-studies %att; >
<!ELEMENT m3-quality ((leaf | node-extension)* , m3-2-body-of-data? ,
m3-3-key-literature-references?)>

<!ATTLIST m3-quality %att; >
<!ELEMENT m3-2-body-of-data ((leaf | node-extension)* , m3-2-s-drug-
substance* , m3-2-p-drug-product* , m3-2-a-appendices? , m3-2-r-
regional-information?)>

<!ATTLIST m3-2-body-of-data %att; >
<!ELEMENT m3-2-s-drug-substance ((leaf | node-extension)* , m3-2-s-1-
general-information? , m3-2-s-2-manufacture? , m3-2-s-3-
characterisation? , m3-2-s-4-control-of-drug-substance? , m3-2-s-5-
reference-standards-or-materials? , m3-2-s-6-container-closure-system? ,
m3-2-s-7-stability?)>

<!ATTLIST m3-2-s-drug-substance %att;
substance CDATA #REQUIRED
manufacturer CDATA #REQUIRED >
<!ELEMENT m3-2-s-1-general-information ((leaf | node-extension)* , m3-2-
s-1-1-nomenclature? , m3-2-s-1-2-structure? , m3-2-s-1-3-general-
properties?)>

<!ATTLIST m3-2-s-1-general-information %att; >
<!ELEMENT m3-2-s-1-1-nomenclature ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-1-1-nomenclature %att; >
<!ELEMENT m3-2-s-1-2-structure ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-1-2-structure %att; >
<!ELEMENT m3-2-s-1-3-general-properties ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-1-3-general-properties %att; >
<!ELEMENT m3-2-s-2-manufacture ((leaf | node-extension)* , m3-2-s-2-1-
manufacturers? , m3-2-s-2-2-description-of-manufacturing-process-and-
process-controls? , m3-2-s-2-3-control-of-materials? , m3-2-s-2-4-
controls-of-critical-steps-and-intermediates? , m3-2-s-2-5-process-
validation-and-or-evaluation? , m3-2-s-2-6-manufacturing-process-
development?)>

<!ATTLIST m3-2-s-2-manufacture %att; >
<!ELEMENT m3-2-s-2-1-manufacturers ((leaf | node-extension)*)>

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<!ATTLIST m3-2-s-2-1-manufacturers %att; >
<!ELEMENT m3-2-s-2-2-description-of-manufacturing-process-and-process-
controls ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-2-2-description-of-manufacturing-process-and-process-
controls %att; >
<!ELEMENT m3-2-s-2-3-control-of-materials ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-2-3-control-of-materials %att; >
<!ELEMENT m3-2-s-2-4-controls-of-critical-steps-and-intermediates ((leaf
| node-extension)*)>

<!ATTLIST m3-2-s-2-4-controls-of-critical-steps-and-intermediates %att;
>
<!ELEMENT m3-2-s-2-5-process-validation-and-or-evaluation ((leaf | node-
extension)*)>

<!ATTLIST m3-2-s-2-5-process-validation-and-or-evaluation %att; >
<!ELEMENT m3-2-s-2-6-manufacturing-process-development ((leaf | node-
extension)*)>

<!ATTLIST m3-2-s-2-6-manufacturing-process-development %att; >
<!ELEMENT m3-2-s-3-characterisation ((leaf | node-extension)* , m3-2-s-
3-1-elucidation-of-structure-and-other-characteristics? , m3-2-s-3-2-
impurities?)>

<!ATTLIST m3-2-s-3-characterisation %att; >
<!ELEMENT m3-2-s-3-1-elucidation-of-structure-and-other-characteristics
((leaf | node-extension)*)>

<!ATTLIST m3-2-s-3-1-elucidation-of-structure-and-other-characteristics
%att; >
<!ELEMENT m3-2-s-3-2-impurities ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-3-2-impurities %att; >
<!ELEMENT m3-2-s-4-control-of-drug-substance ((leaf | node-extension)* ,
m3-2-s-4-1-specification? , m3-2-s-4-2-analytical-procedures? , m3-2-s-
4-3-validation-of-analytical-procedures? , m3-2-s-4-4-batch-analyses? ,
m3-2-s-4-5-justification-of-specification?)>

<!ATTLIST m3-2-s-4-control-of-drug-substance %att; >
<!ELEMENT m3-2-s-4-1-specification ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-4-1-specification %att; >
<!ELEMENT m3-2-s-4-2-analytical-procedures ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-4-2-analytical-procedures %att; >
<!ELEMENT m3-2-s-4-3-validation-of-analytical-procedures ((leaf | node-
extension)*)>

<!ATTLIST m3-2-s-4-3-validation-of-analytical-procedures %att; >
<!ELEMENT m3-2-s-4-4-batch-analyses ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-4-4-batch-analyses %att; >
<!ELEMENT m3-2-s-4-5-justification-of-specification ((leaf | node-
extension)*)>

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<!ATTLIST m3-2-s-4-5-justification-of-specification %att; >
<!ELEMENT m3-2-s-5-reference-standards-or-materials ((leaf | node-
extension)*)>

<!ATTLIST m3-2-s-5-reference-standards-or-materials %att; >
<!ELEMENT m3-2-s-6-container-closure-system ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-6-container-closure-system %att; >
<!ELEMENT m3-2-s-7-stability ((leaf | node-extension)* , m3-2-s-7-1-
stability-summary-and-conclusions? , m3-2-s-7-2-post-approval-stability-
protocol-and-stability-commitment? , m3-2-s-7-3-stability-data?)>

<!ATTLIST m3-2-s-7-stability %att; >
<!ELEMENT m3-2-s-7-1-stability-summary-and-conclusions ((leaf | node-
extension)*)>

<!ATTLIST m3-2-s-7-1-stability-summary-and-conclusions %att; >
<!ELEMENT m3-2-s-7-2-post-approval-stability-protocol-and-stability-
commitment ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-7-2-post-approval-stability-protocol-and-stability-
commitment %att; >
<!ELEMENT m3-2-s-7-3-stability-data ((leaf | node-extension)*)>

<!ATTLIST m3-2-s-7-3-stability-data %att; >
<!ELEMENT m3-2-p-drug-product ((leaf | node-extension)* , m3-2-p-1-
description-and-composition-of-the-drug-product? , m3-2-p-2-
pharmaceutical-development? , m3-2-p-3-manufacture? , m3-2-p-4-control-
of-excipients? , m3-2-p-5-control-of-drug-product? , m3-2-p-6-reference-
standards-or-materials? , m3-2-p-7-container-closure-system? , m3-2-p-8-
stability?)>

<!ATTLIST m3-2-p-drug-product %att;
                                product-name CDATA #IMPLIED
                                dosageform CDATA #IMPLIED >
<!ELEMENT m3-2-p-1-description-and-composition-of-the-drug-product
((leaf | node-extension)*)>

<!ATTLIST m3-2-p-1-description-and-composition-of-the-drug-product
%att; >
<!ELEMENT m3-2-p-2-pharmaceutical-development ((leaf | node-extension)*
, m3-2-p-2-1-components-of-the-drug-product? , m3-2-p-2-2-drug-product?
, m3-2-p-2-3-manufacturing-process-development? , m3-2-p-2-4-container-
closure-system? , m3-2-p-2-5-microbiological-attributes? , m3-2-p-2-6-
compatibility?)>

<!ATTLIST m3-2-p-2-pharmaceutical-development %att; >
<!ELEMENT m3-2-p-2-1-components-of-the-drug-product ((leaf | node-
extension)* , m3-2-p-2-1-1-drug-substance , m3-2-p-2-1-2-excipients)>

<!ATTLIST m3-2-p-2-1-components-of-the-drug-product %att; >
<!ELEMENT m3-2-p-2-1-1-drug-substance ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-1-1-drug-substance %att; >
<!ELEMENT m3-2-p-2-1-2-excipients ((leaf | node-extension)*)>

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<!ATTLIST m3-2-p-2-1-2-excipients %att; >
<!ELEMENT m3-2-p-2-2-drug-product ((leaf | node-extension)* , m3-2-p-2-2-1-formulation-development? , m3-2-p-2-2-2-overages? , m3-2-p-2-2-3-physicochemical-and-biological-properties?)>

<!ATTLIST m3-2-p-2-2-drug-product %att; >
<!ELEMENT m3-2-p-2-2-1-formulation-development ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-2-1-formulation-development %att; >
<!ELEMENT m3-2-p-2-2-2-overages ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-2-2-overages %att; >
<!ELEMENT m3-2-p-2-2-3-physicochemical-and-biological-properties ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-2-3-physicochemical-and-biological-properties %att; >
<!ELEMENT m3-2-p-2-3-manufacturing-process-development ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-3-manufacturing-process-development %att; >
<!ELEMENT m3-2-p-2-4-container-closure-system ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-4-container-closure-system %att; >
<!ELEMENT m3-2-p-2-5-microbiological-attributes ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-5-microbiological-attributes %att; >
<!ELEMENT m3-2-p-2-6-compatibility ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-2-6-compatibility %att; >
<!ELEMENT m3-2-p-3-manufacture ((leaf | node-extension)* , m3-2-p-3-1-manufacturers? , m3-2-p-3-2-batch-formula? , m3-2-p-3-3-description-of-manufacturing-process-and-process-controls? , m3-2-p-3-4-controls-of-critical-steps-and-intermediates? , m3-2-p-3-5-process-validation-and-or-evaluation?)>

<!ATTLIST m3-2-p-3-manufacture %att; >
<!ELEMENT m3-2-p-3-1-manufacturers ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-3-1-manufacturers %att; >
<!ELEMENT m3-2-p-3-2-batch-formula ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-3-2-batch-formula %att; >
<!ELEMENT m3-2-p-3-3-description-of-manufacturing-process-and-process-controls ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-3-3-description-of-manufacturing-process-and-process-controls %att; >
<!ELEMENT m3-2-p-3-4-controls-of-critical-steps-and-intermediates ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-3-4-controls-of-critical-steps-and-intermediates %att; >

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<!ELEMENT m3-2-p-3-5-process-validation-and-or-evaluation ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-3-5-process-validation-and-or-evaluation %att; >
<!ELEMENT m3-2-p-4-control-of-excipients ((leaf | node-extension)* , m3-
2-p-4-1-specifications? , m3-2-p-4-2-analytical-procedures? , m3-2-p-4-
3-validation-of-analytical-procedures? , m3-2-p-4-4-justification-of-
specifications? , m3-2-p-4-5-excipients-of-human-or-animal-origin? , m3-
2-p-4-6-novel-excipient?)>

<!ATTLIST m3-2-p-4-control-of-excipients %att; >
<!ELEMENT m3-2-p-4-1-specifications ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-4-1-specifications %att; >
<!ELEMENT m3-2-p-4-2-analytical-procedures ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-4-2-analytical-procedures %att; >
<!ELEMENT m3-2-p-4-3-validation-of-analytical-procedures ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-4-3-validation-of-analytical-procedures %att; >
<!ELEMENT m3-2-p-4-4-justification-of-specifications ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-4-4-justification-of-specifications %att; >
<!ELEMENT m3-2-p-4-5-excipients-of-human-or-animal-origin ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-4-5-excipients-of-human-or-animal-origin %att; >
<!ELEMENT m3-2-p-4-6-novel-excipient ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-4-6-novel-excipient %att; >
<!ELEMENT m3-2-p-5-control-of-drug-product ((leaf | node-extension)* ,
m3-2-p-5-1-specifications? , m3-2-p-5-2-analytical-procedures? , m3-2-p-
5-3-validation-of-analytical-procedures? , m3-2-p-5-4-batch-analyses? ,
m3-2-p-5-5-characterisation-of-impurities? , m3-2-p-5-6-justification-
of-specifications?)>

<!ATTLIST m3-2-p-5-control-of-drug-product %att; >
<!ELEMENT m3-2-p-5-1-specifications ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-5-1-specifications %att; >
<!ELEMENT m3-2-p-5-2-analytical-procedures ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-5-2-analytical-procedures %att; >
<!ELEMENT m3-2-p-5-3-validation-of-analytical-procedures ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-5-3-validation-of-analytical-procedures %att; >
<!ELEMENT m3-2-p-5-4-batch-analyses ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-5-4-batch-analyses %att; >
<!ELEMENT m3-2-p-5-5-characterisation-of-impurities ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-5-5-characterisation-of-impurities %att; >

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<!ELEMENT m3-2-p-5-6-justification-of-specifications ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-5-6-justification-of-specifications %att; >
<!ELEMENT m3-2-p-6-reference-standards-or-materials ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-6-reference-standards-or-materials %att; >
<!ELEMENT m3-2-p-7-container-closure-system ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-7-container-closure-system %att; >
<!ELEMENT m3-2-p-8-stability ((leaf | node-extension)* , m3-2-p-8-1-
stability-summary-and-conclusion? , m3-2-p-8-2-post-approval-stability-
protocol-and-stability-commitment? , m3-2-p-8-3-stability-data?)>

<!ATTLIST m3-2-p-8-stability %att; >
<!ELEMENT m3-2-p-8-1-stability-summary-and-conclusion ((leaf | node-
extension)*)>

<!ATTLIST m3-2-p-8-1-stability-summary-and-conclusion %att; >
<!ELEMENT m3-2-p-8-2-post-approval-stability-protocol-and-stability-
commitment ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-8-2-post-approval-stability-protocol-and-stability-
commitment %att; >
<!ELEMENT m3-2-p-8-3-stability-data ((leaf | node-extension)*)>

<!ATTLIST m3-2-p-8-3-stability-data %att; >
<!ELEMENT m3-2-a-appendices ((leaf | node-extension)* , m3-2-a-1-
facilities-and-equipment? , m3-2-a-2-adventitious-agents-safety-
evaluation? , m3-2-a-3-novel-excipients?)>

<!ATTLIST m3-2-a-appendices %att; >
<!ELEMENT m3-2-a-1-facilities-and-equipment ((leaf | node-extension)*)>

<!ATTLIST m3-2-a-1-facilities-and-equipment %att; >
<!ELEMENT m3-2-a-2-adventitious-agents-safety-evaluation ((leaf | node-
extension)*)>

<!ATTLIST m3-2-a-2-adventitious-agents-safety-evaluation %att; >
<!ELEMENT m3-2-a-3-novel-excipients ((leaf | node-extension)*)>

<!ATTLIST m3-2-a-3-novel-excipients %att; >
<!ELEMENT m3-2-r-regional-information ((leaf | node-extension)*)>

<!ATTLIST m3-2-r-regional-information %att; >
<!ELEMENT m3-3-key-literature-references ((leaf | node-extension)*)>

<!ATTLIST m3-3-key-literature-references %att; >
<!ELEMENT m4-nonclinical-study-reports ((leaf | node-extension)* , m4-2-
study-reports? , m4-3-copies-of-literature-references?)>

<!ATTLIST m4-nonclinical-study-reports %att; >
<!ELEMENT m4-2-study-reports ((leaf | node-extension)* , m4-2-1-
pharmacology? , m4-2-2-pharmacokinetics? , m4-2-3-toxicology? , m4-2-4-
local-tolerance? , m4-2-5-other-toxicity-studies?)>

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<!ATTLIST m4-2-study-reports %att; >
<!ELEMENT m4-2-1-pharmacology ((leaf | node-extension)* , m4-2-1-1-
primary-pharmacodynamic? , m4-2-1-2-secondary-pharmacodynamic? , m4-2-1-
3-safety-pharmacology? , m4-2-1-4-pharmacodynamic-drug-interactions?)>

<!ATTLIST m4-2-1-pharmacology %att; >
<!ELEMENT m4-2-1-1-primary-pharmacodynamic ((leaf | node-extension)*)>

<!ATTLIST m4-2-1-1-primary-pharmacodynamic %att; >
<!ELEMENT m4-2-1-2-secondary-pharmacodynamic ((leaf | node-extension)*)>

<!ATTLIST m4-2-1-2-secondary-pharmacodynamic %att; >
<!ELEMENT m4-2-1-3-safety-pharmacology ((leaf | node-extension)*)>

<!ATTLIST m4-2-1-3-safety-pharmacology %att; >
<!ELEMENT m4-2-1-4-pharmacodynamic-drug-interactions ((leaf | node-
extension)*)>

<!ATTLIST m4-2-1-4-pharmacodynamic-drug-interactions %att; >
<!ELEMENT m4-2-2-pharmacokinetics ((leaf | node-extension)* , m4-2-2-1-
analytical-methods-and-validation-reports? , m4-2-2-2-absorption? , m4-
2-2-3-distribution? , m4-2-2-4-metabolism? , m4-2-2-5-excretion? , m4-2-
2-6-pharmacokinetic-drug-interactions? , m4-2-2-7-other-pharmacokinetic-
studies?)>

<!ATTLIST m4-2-2-pharmacokinetics %att; >
<!ELEMENT m4-2-2-1-analytical-methods-and-validation-reports ((leaf |
node-extension)*)>

<!ATTLIST m4-2-2-1-analytical-methods-and-validation-reports %att; >
<!ELEMENT m4-2-2-2-absorption ((leaf | node-extension)*)>

<!ATTLIST m4-2-2-2-absorption %att; >
<!ELEMENT m4-2-2-3-distribution ((leaf | node-extension)*)>

<!ATTLIST m4-2-2-3-distribution %att; >
<!ELEMENT m4-2-2-4-metabolism ((leaf | node-extension)*)>

<!ATTLIST m4-2-2-4-metabolism %att; >
<!ELEMENT m4-2-2-5-excretion ((leaf | node-extension)*)>

<!ATTLIST m4-2-2-5-excretion %att; >
<!ELEMENT m4-2-2-6-pharmacokinetic-drug-interactions ((leaf | node-
extension)*)>

<!ATTLIST m4-2-2-6-pharmacokinetic-drug-interactions %att; >
<!ELEMENT m4-2-2-7-other-pharmacokinetic-studies ((leaf | node-
extension)*)>

<!ATTLIST m4-2-2-7-other-pharmacokinetic-studies %att; >
<!ELEMENT m4-2-3-toxicology ((leaf | node-extension)* , m4-2-3-1-single-
dose-toxicity? , m4-2-3-2-repeat-dose-toxicity? , m4-2-3-3-genotoxicity?
, m4-2-3-4-carcinogenicity? , m4-2-3-5-reproductive-and-developmental-
toxicity)>

<!ATTLIST m4-2-3-toxicology %att; >
<!ELEMENT m4-2-3-1-single-dose-toxicity ((leaf | node-extension)*)>

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<!ATTLIST m4-2-3-1-single-dose-toxicity %att; >
<!ELEMENT m4-2-3-2-repeat-dose-toxicity ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-2-repeat-dose-toxicity %att; >
<!ELEMENT m4-2-3-3-genotoxicity ((leaf | node-extension)* , m4-2-3-3-1-
in-vitro? , m4-2-3-3-2-in-vivo?)>

<!ATTLIST m4-2-3-3-genotoxicity %att; >
<!ELEMENT m4-2-3-3-1-in-vitro ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-3-1-in-vitro %att; >
<!ELEMENT m4-2-3-3-2-in-vivo ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-3-2-in-vivo %att; >
<!ELEMENT m4-2-3-4-carcinogenicity ((leaf | node-extension)* , m4-2-3-4-
1-long-term-studies? , m4-2-3-4-2-short-or-medium-term-studies? , m4-2-
3-4-3-other-studies?)>

<!ATTLIST m4-2-3-4-carcinogenicity %att; >
<!ELEMENT m4-2-3-4-1-long-term-studies ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-4-1-long-term-studies %att; >
<!ELEMENT m4-2-3-4-2-short-or-medium-term-studies ((leaf | node-
extension)*)>

<!ATTLIST m4-2-3-4-2-short-or-medium-term-studies %att; >
<!ELEMENT m4-2-3-4-3-other-studies ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-4-3-other-studies %att; >
<!ELEMENT m4-2-3-5-reproductive-and-developmental-toxicity ((leaf |
node-extension)* , m4-2-3-5-1-fertility-and-early-embryonic-development?
, m4-2-3-5-2-embryo-fetal-development? , m4-2-3-5-3-prenatal-and-
postnatal-development-including-maternal-function? , m4-2-3-5-4-studies-
in-which-the-offspring-junenile-animals-are-dosed-and-or-further-
evaluated?)>

<!ATTLIST m4-2-3-5-reproductive-and-developmental-toxicity %att; >
<!ELEMENT m4-2-3-5-1-fertility-and-early-embryonic-development ((leaf |
node-extension)*)>

<!ATTLIST m4-2-3-5-1-fertility-and-early-embryonic-development %att; >
<!ELEMENT m4-2-3-5-2-embryo-fetal-development ((leaf | node-
extension)*)>

<!ATTLIST m4-2-3-5-2-embryo-fetal-development %att; >
<!ELEMENT m4-2-3-5-3-prenatal-and-postnatal-development-including-
maternal-function ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-5-3-prenatal-and-postnatal-development-including-
maternal-function %att; >
<!ELEMENT m4-2-3-5-4-studies-in-which-the-offspring-junenile-animals-
are-dosed-and-or-further-evaluated ((leaf | node-extension)*)>

<!ATTLIST m4-2-3-5-4-studies-in-which-the-offspring-junenile-animals-
are-dosed-and-or-further-evaluated %att; >
<!ELEMENT m4-2-4-local-tolerance ((leaf | node-extension)*)>

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<!ATTLIST m4-2-4-local-tolerance %att; >
<!ELEMENT m4-2-5-other-toxicity-studies ((leaf | node-extension)* , m4-
2-5-1-antigenicity? , m4-2-5-2-immunotoxicity? , m4-2-5-3-mechanistic-
studies? , m4-2-5-4-dependence? , m4-2-5-5-metabolites? , m4-2-5-6-
impurities? , m4-2-5-7-other?)>

<!ATTLIST m4-2-5-other-toxicity-studies %att; >
<!ELEMENT m4-2-5-1-antigenicity ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-1-antigenicity %att; >
<!ELEMENT m4-2-5-2-immunotoxicity ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-2-immunotoxicity %att; >
<!ELEMENT m4-2-5-3-mechanistic-studies ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-3-mechanistic-studies %att; >
<!ELEMENT m4-2-5-4-dependence ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-4-dependence %att; >
<!ELEMENT m4-2-5-5-metabolites ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-5-metabolites %att; >
<!ELEMENT m4-2-5-6-impurities ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-6-impurities %att; >
<!ELEMENT m4-2-5-7-other ((leaf | node-extension)*)>

<!ATTLIST m4-2-5-7-other %att; >
<!ELEMENT m4-3-copies-of-literature-references ((leaf | node-
extension)*)>

<!ATTLIST m4-3-copies-of-literature-references %att; >
<!ELEMENT m5-clinical-study-reports ((leaf | node-extension)* , m5-2-
tabular-listing-of-all-clinical-studies? , m5-3-clinical-study-reports?
, m5-4-literature-references?)>

<!ATTLIST m5-clinical-study-reports %att; >
<!ELEMENT m5-2-tabular-listing-of-all-clinical-studies ((leaf | node-
extension)*)>

<!ATTLIST m5-2-tabular-listing-of-all-clinical-studies %att; >
<!ELEMENT m5-3-clinical-study-reports ((leaf | node-extension)* , m5-3-
1-reports-of-biopharmaceutic-studies? , m5-3-2-reports-of-studies-
pertinent-to-pharmacokinetics-using-human-biomaterials? , m5-3-3-
reports-of-human-pharmacokinetic-pk-studies? , m5-3-4-reports-of-human-
pharmacodynamic-pd-studies? , m5-3-5-reports-of-efficacy-and-safety-
studies* , m5-3-6-reports-of-post-marketing-experience? , m5-3-7-case-
report-forms-and-individual-patient-listings?)>

<!ATTLIST m5-3-clinical-study-reports %att; >
<!ELEMENT m5-3-1-reports-of-biopharmaceutic-studies ((leaf | node-
extension)* , m5-3-1-1-bioavailability-ba-study-reports? , m5-3-1-2-
comparative-ba-and-bioequivalence-be-study-reports? , m5-3-1-3-invitro-
in-vivo-correlation-study-reports? , m5-3-1-4-reports-of-bioanalytical-
and-analytical-methods-for-human-studies?)>

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<!ATTLIST m5-3-1-reports-of-biopharmaceutic-studies %att; >
<!ELEMENT m5-3-1-1-bioavailability-ba-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-1-1-bioavailability-ba-study-reports %att; >
<!ELEMENT m5-3-1-2-comparative-ba-and-bioequivalence-be-study-reports
((leaf | node-extension)*)>

<!ATTLIST m5-3-1-2-comparative-ba-and-bioequivalence-be-study-reports
%att; >
<!ELEMENT m5-3-1-3-invivo-invitro-correlation-study-reports ((leaf |
node-extension)*)>

<!ATTLIST m5-3-1-3-invivo-invitro-correlation-study-reports %att; >
<!ELEMENT m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-
human-studies ((leaf | node-extension)*)>

<!ATTLIST m5-3-1-4-reports-of-bioanalytical-and-analytical-methods-for-
human-studies %att; >
<!ELEMENT m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-
human-biomaterials ((leaf | node-extension)* , m5-3-2-1-plasma-protein-
binding-study-reports? , m5-3-2-2-reports-of-hepatic-metabolism-and-
drug-interaction-studies? , m5-3-2-3-reports-of-studies-using-other-
human-biomaterials?)>

<!ATTLIST m5-3-2-reports-of-studies-pertinent-to-pharmacokinetics-using-
human-biomaterials %att; >
<!ELEMENT m5-3-2-1-plasma-protein-binding-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-2-1-plasma-protein-binding-study-reports %att; >
<!ELEMENT m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-
studies ((leaf | node-extension)*)>

<!ATTLIST m5-3-2-2-reports-of-hepatic-metabolism-and-drug-interaction-
studies %att; >
<!ELEMENT m5-3-2-3-reports-of-studies-using-other-human-biomaterials
((leaf | node-extension)*)>

<!ATTLIST m5-3-2-3-reports-of-studies-using-other-human-biomaterials
%att; >
<!ELEMENT m5-3-3-reports-of-human-pharmacokinetic-pk-studies ((leaf |
node-extension)* , m5-3-3-1-healthy-subject-pk-and-initial-tolerability-
study-reports? , m5-3-3-2-patient-pk-and-initial-tolerability-study-
reports? , m5-3-3-3-intrinsic-factor-pk-study-reports? , m5-3-3-4-
extrinsic-factor-pk-study-reports? , m5-3-3-5-population-pk-study-
reports?)>

<!ATTLIST m5-3-3-reports-of-human-pharmacokinetic-pk-studies %att; >
<!ELEMENT m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-
reports ((leaf | node-extension)*)>

<!ATTLIST m5-3-3-1-healthy-subject-pk-and-initial-tolerability-study-
reports %att; >
<!ELEMENT m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
((leaf | node-extension)*)>

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<!ATTLIST m5-3-3-2-patient-pk-and-initial-tolerability-study-reports
%att; >
<!ELEMENT m5-3-3-3-intrinsic-factor-pk-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-3-3-intrinsic-factor-pk-study-reports %att; >
<!ELEMENT m5-3-3-4-extrinsic-factor-pk-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-3-4-extrinsic-factor-pk-study-reports %att; >
<!ELEMENT m5-3-3-5-population-pk-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-3-5-population-pk-study-reports %att; >
<!ELEMENT m5-3-4-reports-of-human-pharmacodynamic-pd-studies ((leaf |
node-extension)* , m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports?
, m5-3-4-2-patient-pd-and-pk-pd-study-reports?)>

<!ATTLIST m5-3-4-reports-of-human-pharmacodynamic-pd-studies %att; >
<!ELEMENT m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports ((leaf |
node-extension)*)>

<!ATTLIST m5-3-4-1-healthy-subject-pd-and-pk-pd-study-reports %att; >
<!ELEMENT m5-3-4-2-patient-pd-and-pk-pd-study-reports ((leaf | node-
extension)*)>

<!ATTLIST m5-3-4-2-patient-pd-and-pk-pd-study-reports %att; >
<!ELEMENT m5-3-5-reports-of-efficacy-and-safety-studies ((leaf | node-
extension)* , m5-3-5-1-study-reports-of-controlled-clinical-studies-
pertinent-to-the-claimed-indication? , m5-3-5-2-study-reports-of-
uncontrolled-clinical-studies? , m5-3-5-3-reports-of-analyses-of-data-
from-more-than-one-study? , m5-3-5-4-other-study-reports?)>

<!ATTLIST m5-3-5-reports-of-efficacy-and-safety-studies %att;
indication
CDATA #IMPLIED >
<!ELEMENT m5-3-5-1-study-reports-of-controlled-clinical-studies-
pertinent-to-the-claimed-indication ((leaf | node-extension)*)>

<!ATTLIST m5-3-5-1-study-reports-of-controlled-clinical-studies-
pertinent-to-the-claimed-indication %att; >
<!ELEMENT m5-3-5-2-study-reports-of-uncontrolled-clinical-studies ((leaf
| node-extension)*)>

<!ATTLIST m5-3-5-2-study-reports-of-uncontrolled-clinical-studies %att;
>
<!ELEMENT m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
((leaf | node-extension)*)>

<!ATTLIST m5-3-5-3-reports-of-analyses-of-data-from-more-than-one-study
%att; >
<!ELEMENT m5-3-5-4-other-study-reports ((leaf | node-extension)*)>

<!ATTLIST m5-3-5-4-other-study-reports %att; >
<!ELEMENT m5-3-6-reports-of-post-marketing-experience ((leaf | node-
extension)*)>

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<!--ATTLIST m5-3-6-reports-of-post-marketing-experience %att; -->
<!--ELEMENT m5-3-7-case-report-forms-and-individual-patient-listings
((leaf | node-extension)*)-->

<!--ATTLIST m5-3-7-case-report-forms-and-individual-patient-listings
%att; -->
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## **Appendix 15 Glossary**

The intended content of this section is the definition of terms used in the set of documentation associated with the eCTD. The initial starting point for this is the existing ESTRi Glossary which has been included. This draft identifies those terms that are expected to be included.

### **Application**

A software program that performs a specific function.

### **Application Program Interface (API)**

A set of routines used by an application program to request or execute functions performed by the operating system or another application program.

### **Architecture**

A general term for the design and construction of computer systems, including technical infrastructure, information (data), and applications.

### **ASCII**

American Standard Code for Information Interchange. A specification for representing text as computer-readable information.

### **Authentication**

A security mechanism which verifies the identity of the sender of a message over a network.

### **Browser**

A program which allows the user to read hypertext, to view contents of web pages, and to navigate from one page to another, e.g., Netscape Navigator, Mosaic, Microsoft Internet Explorer.

### **CA**

Certification Authority. An agency which is trusted by a group of users of encryption technology to store and disseminate the private key of other users in the group.

### **Client**

A computer program (or process) that requests a service of another computer program (or process), called a server. The server program may exist on the same computer or on another computer on a network.

### **Client/Server computing**

A processing environment in which personal computers or other workstations, acting as clients, cooperate with one or more main processing units, acting as servers, to accomplish whatever tasks need to be done.

### **Common Technical Document (CTD)**

Definition to be added

**Computing environment**

The set of hardware and software that enables the end-user to access IT resources.

**Configuration**

The way in which a computer and its peripherals (printers, modems, etc.) are connected in a system, especially the firmware (refer to definition later in glossary) settings of its internal components such as memory size and video mode.

**Connectivity**

The factors (hardware, software, infrastructure) which facilitate the sharing of information between one or more technical environments.

**Database**

One or more large structured sets of persistent data, usually associated with software to update and query the data.

**Database Management System (DBMS)**

Widely used in business applications, a suite of programs which typically manage large structured sets of persistent data, offering query facilities to many users.

**Decryption**

To reverse encryption.

**Dedicated line**

A communications line that is used solely for computer connections; a telephone line leased expressly for the purpose of linking two users more-or-less permanently, generally to produce digital transmissions at a faster rate. If you buy an additional phone line for your modem, that is a dedicated line.

**DES**

Data Encryption Standard based on a symmetric algorithm.

**De facto standard**

A 'standard' which is in such widespread use that it is accepted as a standard but which has not been ratified by any official standards body, such as the ISO.

**DTD**

Document Type Definition. A hierarchical organization or representation of the information contents of a document utilized by SGML or XML.

**eCTD**

The electronic format of the ICH Common Technical Document

**E-mail**

Electronic mail; the service that allows users to compose, edit, send, read, forward, and store messages using mail software and word processing capability on a computer.

**Encryption**

The process of reversibly confusing text or data using a secret formula.

**ESTRI**

Electronic Standards for the Transfer of Regulatory Information.

**EWG**

Expert Working Group.

**Firmware**

Programming that is a permanent part of a computing device.

**Hardware**

The physical components of a computer system such as the system units, monitor, modem, printer, keyboard, and drives.

**Hardware platform**

A specific computer processing system.

**Header**

Information placed in front of a message which ensures that the message is routed to its destination and that it can be opened and read by the receiving software.

**HTML**

Hypertext Markup Language. Commonly used to format Web pages.

**Hypertext**

A system that enables links to be established between specific words or figures in a document to other text, tables or image allowing quick access to the linked items (such as on the World Wide Web).

**ICH**

International Conference on Harmonization of .Technical Requirements for Registration of Pharmaceuticals for Human Use.

**Information**

Any representation of knowledge such as facts, data, or opinions in any medium or form, including textual, numerical, graphic, cartographic, narrative, or audio-visual forms.

**Information system (IS)**

A discrete set of information resources organized for the collection, processing, maintenance, transmission, and dissemination of information in accordance with defined procedures.

**Infrastructure**

The basic support services for computing; the hardware, operating system, and network on which applications and data are stored and on which the database management systems run.

**Interface**

A boundary across which two systems communicate; an information interchange path that allows parts of a computer, multiple computers, and external equipment to communicate or interact.

**Internet**

The world-wide network of computers for accessing, sending, sharing, and transferring information between sites at different locations. It is uncontrolled and unadministered, and when you connect to the Internet, you actually become a part of it.

**Interoperability**

The degree or extent to which diverse environments (hardware and software) are able to exchange information without loss of content, and in a manner transparent to the user.

**Intranet**

A closed/private network which supports a distributed system and facilitates the distribution of information within an organization.

**ISO**

International Standards Organization - founded in 1946, it is the principal international standards-setting organization.

**Key**

The code to encrypt and decrypt files; most commonly as a pair called public key and private key.

**Legacy system**

An older computer system or application which remains in use after new versions or applications have been introduced, usually because it contains data on older projects for which it is not cost effective to transfer to the new systems or versions.

**Local Area Network (LAN)**

A data communication network which is limited to a building or a group of buildings in close proximity.

**Migration**

The planned systematic transition from one application or system to another application or system.

**MIME**

Multipurpose Internet Mail Extension - this standard defines the message format for textual messages on the Internet.

## **M2**

Multidisciplinary Group 2 (ESTRI) of ICH.

### **Network**

A communication system which connects different computers and enables them to share peripherals such as printers, disk drives and databases. Users (clients) can access applications and databases connected by the network.

### **PDF**

Portable Document Format - a proprietary (Adobe Systems) de-facto standard for the electronic transfer of documents.

### **Personal Computer (PC)**

A general-purpose single-user microcomputer designed to be operated by one person at a time, e.g., IBM PC, Macintosh, etc.

### **Protocol**

A set of rules to which all IT companies and software products have to adhere; the language spoken between computers to help them exchange information.

### **Server**

The central computer (main processing unit) in a network which provides some service for other computers connected to it.

### **SGML**

Standardized Generalized Markup Language. An ISO standard for describing structured information in a platform independent manner.

### **Software**

Computer programs or applications. There are two principle types - system software, e.g., computer operating system or a utility program (sometimes called a driver) for printing; and application software, e.g., an accounts package or CAD program.

### **Software platform**

The combination of a computer hardware type and its operating system (e.g. Intel Pentium / Windows2000

### **Standard**

A technical specification which addresses a business requirement, has been implemented in viable commercial products, and, to the extent practical, complies with recognized standards organizations such as ISO.

### **TIFF**

Tag Image File Format - a CCITT standard for electronically storing images.

### **Wide Area Network (WAN)**

A network, usually connected in serial lines, extending over areas larger than the LAN, and connecting several distant locations.

**Web page**

Any page on the World Wide Web. The page usually offers the reader ability to jump to other topics of interest.

**World Wide Web (WWW)**

Segment of the Internet offering point and click (hypertext) access to information, as text, image or sound, on an enormous number of topics from around the world.

**XML**

Extensible Markup Language. An ISO standard for describing structured information in a platform independent manner.

Notes for appendix 13. Glossary

The terminology will be harmonized with the rest of the document

Backbone File

Common Formats

character encoding

Checksums

Chemical Markup Language

CML

content

could

Directory Structure

document

eCTD Spacename

eCTD Style Sheets

file

file extension

format

GIF

IMT

Internet Media Type

JPEG

Leaf FileLifecycle Management

MD5

neutral format

Node

Node Index

PDF

PNG

presentation

Regional Formats

Root File  
Root Directory  
RTF  
Scalable Vector Graphics  
should  
SVG  
TIFF  
Transparent Content Negotiation  
spacename  
Unicode  
UTF-8  
XHTML  
XML